# "CLINICO-HAEMATOLOGICAL PROFILE OF PANCYTOPENIA"

***Dissertation submitted to***

***THE TAMIL NADU DR.M.G.R. MEDICAL UNIVERSITY***

***CHENNAI, TAMIL NADU***

***in partial fulfilment for the Degree of***

**DOCTOR OF MEDICINE - BRANCH I GENERAL MEDICINE**

**APRIL 2016**


**TIRUNELVELI MEDICAL COLLEGE HOSPITAL**

**TIRUNELVELI – 11, TAMIL NADU**

# CERTIFICATE

This is to certify that the dissertation entitled **"CLINICO HAEMATOLOGICAL PROFILE OF PANCYTOPENIA"** submitted by **D ALEX MATHEW** to The Tamilnadu Dr. M.G.R. Medical University, Chenna in partial fulfilment for the award of M.D. Degree (GENERAL MEDICINE) is bonafide work carried out by him under my guidance and supervision during tl course of study 2013-2016. This dissertation partially or fully has not bee submitted for any other degree or diploma of this university or other.

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## DECLARATION

I solemnly declare that the dissertation titled "**CLINICO HAEMATOLOGICAL PROFILE OF PANCYTOPENIA**" is prepared b me.

The dissertation is submitted to The Tamilnadu Dr, M.G.R. Medical universi towards the partial fulfilment of requirements for the award of M.D. Degr (Branch I) in General Medicine . I also solemnly declare that this bonafide wo or a part of this work was not submitted by me or any others for any awar degree, diploma to any university, found either in India or abroad.

Place: Tirunelveli.
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| 2. | Study Protocol | ☐ |
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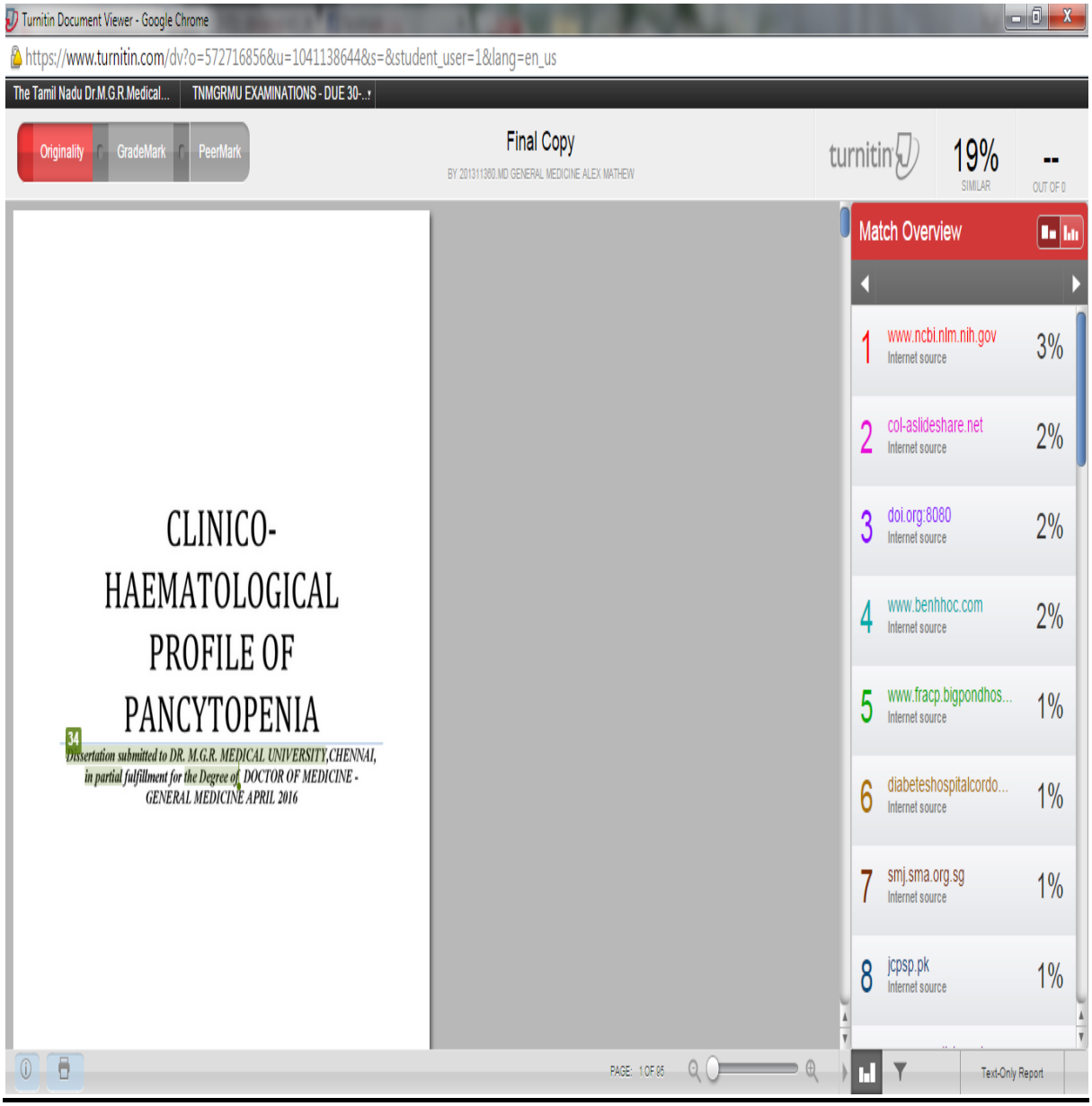
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# INTRODUCTION

Pancytopenia is an important clinico-haematological entity encountered in our day to day clinical practice. There are varying trends in its clinical presentation, treatment approaches and outcome. It is a disorder where all the three major formed elements of blood namely the RBCs, WBCs and platelets are diminished in number. It is not a disease entity, but a triad of findings that may result from a wide number of possible disease processes — that primarily or secondarily involve the bone marrow. The severity of pancytopenia and the underlying pathology plays an important role in determining the treatment approach and response of patient to same. In India, the causes of pancytopenia are not well defined and the present study has been undertaken to evaluate the various causes and to correlate their peripheral blood findings and various haematological parameters to arrive at a specific diagnosis. I hope this data will help in planning the diagnostic and therapeutic approach in patients with pancytopenia.

# REVIEW OF LITERATURE

Pancytopenia is not an uncommon haematological problem which we face in our daily clinical practice and should be suspected whenever a patient presents with prolonged fever, unexplained anemia, and bleeding tendencies.

It is defined as a reduction in all the three types of blood cell lines and thus involves anaemia, leucopenia and thrombocytopenia. It presents with symptoms of bone marrow failure such as pallor, dyspnoea, bleeding, easy bruising and increased propensity for infection. The causes for this condition are many and varied as seen in the study done by Khan et al and includes megaloblastic anaemia, aplastic anaemia, myelodysplasia etc... The incidence of various disorders causing pancytopenia varies with varying geographical distribution and genetic disturbances.

The management and prognosis of pancytopenia depends on the underlying pathology as seen in study by Keisu M, Osta et al[18]. It can either be due to insufficient production of haematopoeitic cells in the bone marrow (as in infections, infiltration by malignant cells or due to effect of toxins) due to ineffective erythropoeisis with a normocellular or hypercellular marrow, without any abnormal cells, (eg- ineffective erythropoeisis and dysplasia), due to arrest in the maturation of cells or due to peripheral sequestration of blood cells.

Bone marrow biopsy plays an important role in the understanding of etiology of pancytopenia in patients who need laboratory workup. Commonly it is done for the evaluation of unexplained cytopenias and malignant conditions like leukemia. Bone marrow biopsy is done at times for diagnosis and staging of

neoplasm and storage disorders. Trephine biopsy is usually performed when there is hypoplasia or aplasia on aspiration.

In study by Kar M etal[16] the commonest cause of pancytopenia was hypoplastic bone marrow followed by haematological malignancies and megaloblastic anemia.

In a study by Memon S et al[10], common clinical presentations were pallor, fever, petechial hemorrhages, organomegaly and epistaxis and gastrointestinal tract bleeding. Infections were the third most common cause of pancytopenia in a study conducted by Gupta et al.

In a study by Talarmin et al[19] vitamin deficiencies were frequent in underdeveloped countries and were responsible for megaloblastic anaemia. The most common findings in the bone marrow evaluation were histiocytic haemophagocytosis and granulomas in a study by Sari I et al.[21]

In a study by Santra G et al, idiopathic aplastic anaemia (20.72 %) was the commonest cause of pancytopenia, followed by hypersplenism due to chronic liver disease (11.71 %). Combined cobalamin and folate deficiency was

seen in 5 patients (3.51%). Cobalamin deficiency was found to be more common in our setting and is largely underdiagnosed in the age of folate supplementation.

Chronic aplastic anaemia may be one among the most common causes of bicytopenia or pancytopaenia during pregnancy, followed by myelodysplastic syndrome as seen in a study by Zhang C, Liang MY and Wang SM.[20]

**Causes of Pancytopenia**

They can be classified either into Primary and Secondary, Or according to cellularity of bone marrow as cellular or hypocellular marrow.

| **Primary** | **Secondary** |
|---|---|
| | Nutritional |
| Idiopathic | Drugs |
| Congenital/ Familial | Viral infections |
| | Mycobacterial infections |
| | Autoimmune disorders |
| | Chemicals (benzene, arsenic) |
| | Cytotoxic drugs |

Malignant infiltration

Paroxysmal nocturnal haemoglobinuria

**Pancytopenia with Cellular Bone Marrow**

| Primary bone marrow diseases | Secondary to systemic diseases |
|---|---|
| Myelodysplasia | SLE |
| Paroxysmal nocturnal haemoglobinuria | Hypersplenism |
| Myelofibrosis | $B_{12}$, Folate deficiency |
| Some aleukemic leukemia | Overwhelming infection |
| Alcohol | Tuberculosis |
| Myelophthisis | Brucellosis |
| Bone marrow lymphoma | Sarcoidosis |
| Hairy cell leukemia | Leishmaniasis |

**Pancytopenia with Hypocellular Bone Marrow**

Constitutional Aplastic Anemia (Fanconi's anemia, dyskeratosis congenita)

Acquired Aplasic Anemia

Some acute lymphoid leukemia

Rare aleukemic leukemia

Some myelodysplasia

Some lymphomas of bone marrow

**Hypocellular Bone marrow with or without Cytopenia**

Anorexia nervosa, starvation

Mycobacterium

Legionnaires' disease

Q Fever

# AIMS, OBJECTIVES &

# METHODOLOGY

# AIMS AND OBJECTIVES

A) To study the various clinical presentations in pancytopenia.

B) To evaluate various hematological parameters and to arrive at a diagnosis

# MATERIALS AND METHODS

Patients admitted in General Medicine Department of Government Medical College, Tirunelveli fulfilling criteria for pancytopenia were evaluated clinically. Adequate haematological investigations and other relevant investigations were carried out. Peripheral smear and bone marrow examination were done if necessary and other investigations were also carried out as a part of the workup.

# STUDY DESIGN

Cross sectional observational study

# SAMPLE SIZE

All cases of pancytopenia in patients admitted in Medicine Department wer evaluated.

# STUDY PERIOD

JULY2014- JUNE2015

# INCLUSION CRITERIA

Case selection was based on clinical features and supported by laboratory evidence, which included peripheral blood counts for haemoglobin, WBCs and platelets. Inclusion criteria were presence of all 3 of the following:

Haemoglobin <10gm/dl

Total WBC count <4,000 / μL

Platelet count <1,00,000/ μL

# EXCLUSION CRITERIA

Patients on chemotherapy

Patients below 13 years of age

# REVIEW OF LITERATURE

## Haematopoiesis[2,4]

Haematopoiesis is a complicated process by which haematopoietic stem cells can both self replicate to maintain a pool of hematopoietic stem cells and also differentiate into myeloid and lymphoid lineage committed hematopoietic progenitor cells, which can further terminally differentiate to produce all the cellular elements of blood.

It is believed that haematopoiesis begins as early as 3rd week after fertilisation, both from aorto-gonadal-mesonephros region and from extra-embryonic mesoderm in yolk sac. This is followed by shift of site of erythropoeisis to the fetal liver and spleen, and fetal liver remains the dominant hematopoietic site in fetal life. By the 5th month of gestation, haematopoiesis gets established in bone marrow. At the time of birth, haematopoietic red bone marrow is found in the medullary cavities of every bone, but as age advances they get replaced by fat/yellow marrow and at adulthood red marrow gets restricted to pelvis, vertebrae, clavicles, ribs, sternum, skull, proximal humeri and upper femora.

## Bone Marrow[2]

Bone marrow is one of the largest organs in the human body approaching size and weight of liver. Normally, WBC producing myeloid series

of cells constitute 75% of cells, while maturing RBCs constitute 25%. This difference is due to difference in lifespan of both RBCs and WBCs.

Haematopoietic stem cells are bone marrow cells that are derived from uncommitted totipotent stem cells, which can form any cell in the body which includes all types of blood cells which can differentiate into a particular type of committed stemcells(progenitor cells) which in turn form various differentiated types of blood cells. There are separate pools of progenitor cells for RBCs, megakaryocytes, lymphocytes, eosinophils and basophils; but neutrophils and monocytes arise from a common precursor cell. Bone marrow stem cells also form the source of osteoclasts, mast cells, dendritic cells, Kupffer cells and Langerhans cells.

## Normal Bone Marrow Structure[4]

The red marrow is interspersed between the trabeculae of bone within the bony cavity. It contains special connective tissue cells, reticulin, blood vessels, fat, nerves and macrophages in addition to cells of the lymphoid and haemopoietic series. A supportive framework is provided by a network of fine reticulin fibrils. These fibrils are produced by the adventitial reticular cells. Arteriolar blood passes into the relatively large lumen of sinusoids which are

lined by a single layer of endothelial cells. Entry of newly formed blood cells into the circulation occurs at this site. Fat cells contribute to approximately half the extra vascular volume of red marrow and nearly all of the extravascular volume of yellow marrow in the peripheral parts of the long bones.

### Ratio

The M: E ratio is based on a count of 200 to 500 marrow cells. In a normal adult the ratio is about 3:1 or 4:1

## Spleen[1]

It forms part of reticuloendothelial system which develops during 5$^{th}$ week of gestation in the dorsal mesogastrium.

### Physiological role

- Maintenance of quality of RBCs by removing senescent & defective ones
- Production of antibodies in white pulp
- Removal of antibody coated bacteria & blood cells

### Adaptive functions of spleen[1]

- Clearance of bacteria and particulate materials from blood
- Immune response generation to pathogens
- Extramedullary hematopoiesis at times of need

Normal human spleen contains significant number of marginated neutrophils and 1/3$^{rd}$ of total body platelets and these sequestrated cells are available when body needs them during bleeding or infection.

## Various Cytokines and the cell lines they stimulate[4]

| Cytokine | Stimulated cell line | Source |
|---|---|---|
| Erythropoietin | Erythrocyte | Kidney and Kupffer cell in liv |
| SCF | Erythrocyte, Granulocyte, Monocyte, Megakaryocyte | Multiple cell types |
| G-CSF | Granulocyte | Fibroblasts, Monocytes, Endothelial cells, |
| GM-CSF | Erythrocyte, Granulocyte, Megakaryocyte | Fibroblasts, Endothelial cells, lymphocytes, Monocytes, |
| M-CSF | Monocyte | Fibroblasts, Endothelial cells, Monocytes |
| Thrombopoietin | Megakaryocyte | Kidney, liver |

| | | |
|---|---|---|
| IL-1 | Erythrocyte, Granulocyte, Monocyte, Megakaryocyte | Multiple cell types |
| IL-3 | Erythrocyte, Granulocyte, Monocyte, Megakaryocyte, | T lymphocytes |
| IL-4 | Basophil | T lymphocytes |
| IL-5 | Eosinophil | T lymhocytes |
| Il-6 | Erythrocyte, Granulocyte, Monocyte, Megakaryocyte, | Endothelial cells, fibroblasts, macrophages |
| IL-7 | B cells | Leukocytes |
| IL-8 | T cells and neutrophi | Leukocytes |
| IL-9 | BFU-E, CFU-GEMM | Lymphocytes |
| IL-11 | Erythrocyte, granulocyte, megakaryocyte | Fibroblasts, osteoblasts |

# ERYTHROPOEISIS[4]

## Stages of development

.CFU-E

· Proerythroblast(least mature form, prominent nucleoli)

· Basophilic erythroblast(maximum ribosomes, chromatin condensation)

· Polychromatic erythroblast(maximum mitochondria)

· Orthochromatic erythroblast_ lose their nucleus

· Reticulocye( Nucleus absent)

· Mature erythrocyte/RBC

# GRANULOPOIESIS[4]

## NEUTROPHIL SERIES

## Stages of development

· Myeloblast (round or oval nucleus with fine chromatin& 1-5 nucleoli)

· Promyelocyte (largest cell with less prominent nucleoli)

· Myelocyte (nuclear indentation & coarse chromatin structure, last cell that is capable of cell division)

· Metamyelocyte ( bean shaped nucleus)

· Band or stab form

· Segmented or polymorphonuclear granulocyte

· Polymorphonuclear eosinophil (bilobed nucleus, basophilic cytoplasm filled with orange red granules)

· Polymorphonucelar Basophil (deeply staining blue to purple metachromatic granules obscuring nucleus & cytoplasm stains reddish pink)

## THE MONOCYTE – MACROPHAGE SERIES[4]

Monoblast (round or oval nucleus with fine chromatin)

Promonocyte (indented nucleus with single nucleoli)

Monocyte (large, lobulated or bean shaped nucleus without nucleoli)

Macrophage (mobile & phagocytic)

## THE LYMPHOID SERIES[4]

Lymphoblast

Large lymphocyte

Small lymphocyte

Plasma cell

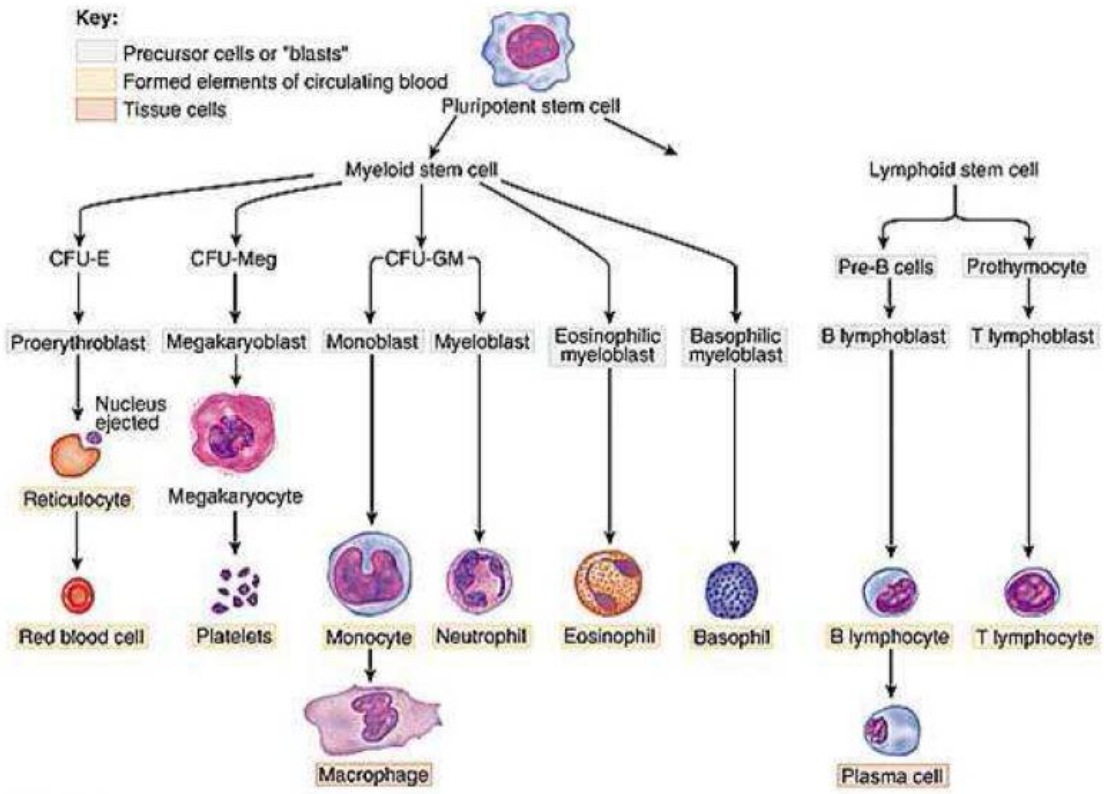
## THE MEGAKARYOCYTIC SERIES[4]

Megakaryoblast

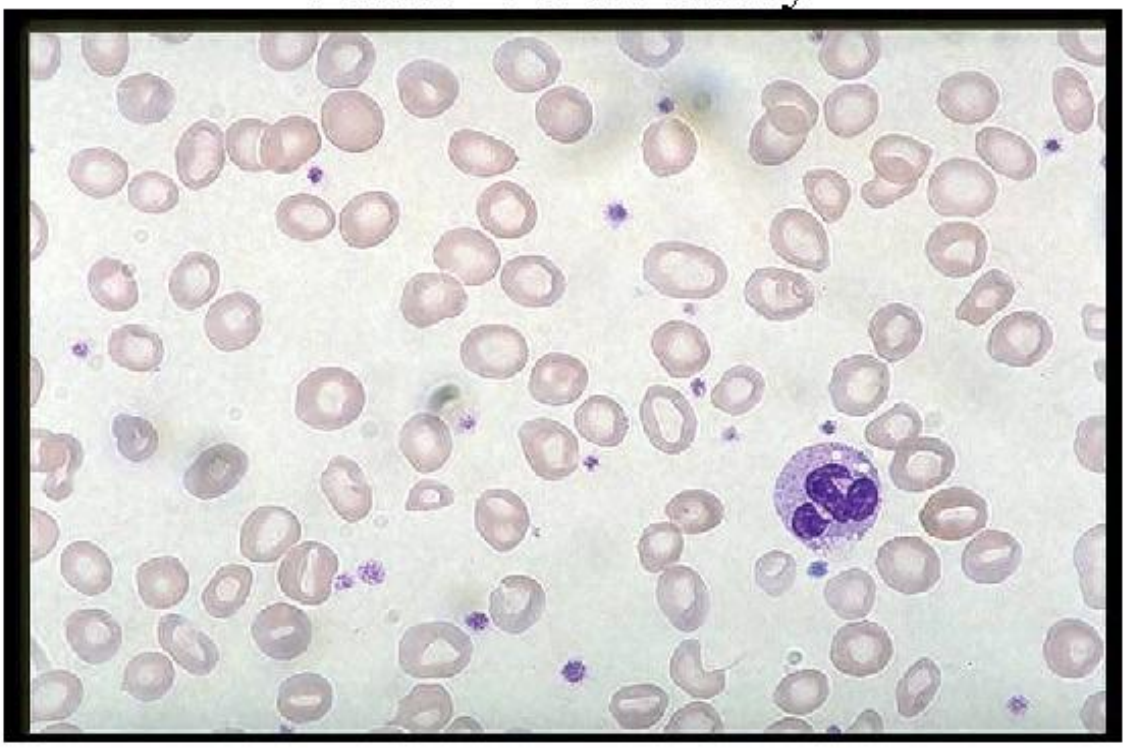
Promegakaryoctye

Megakaryoctye

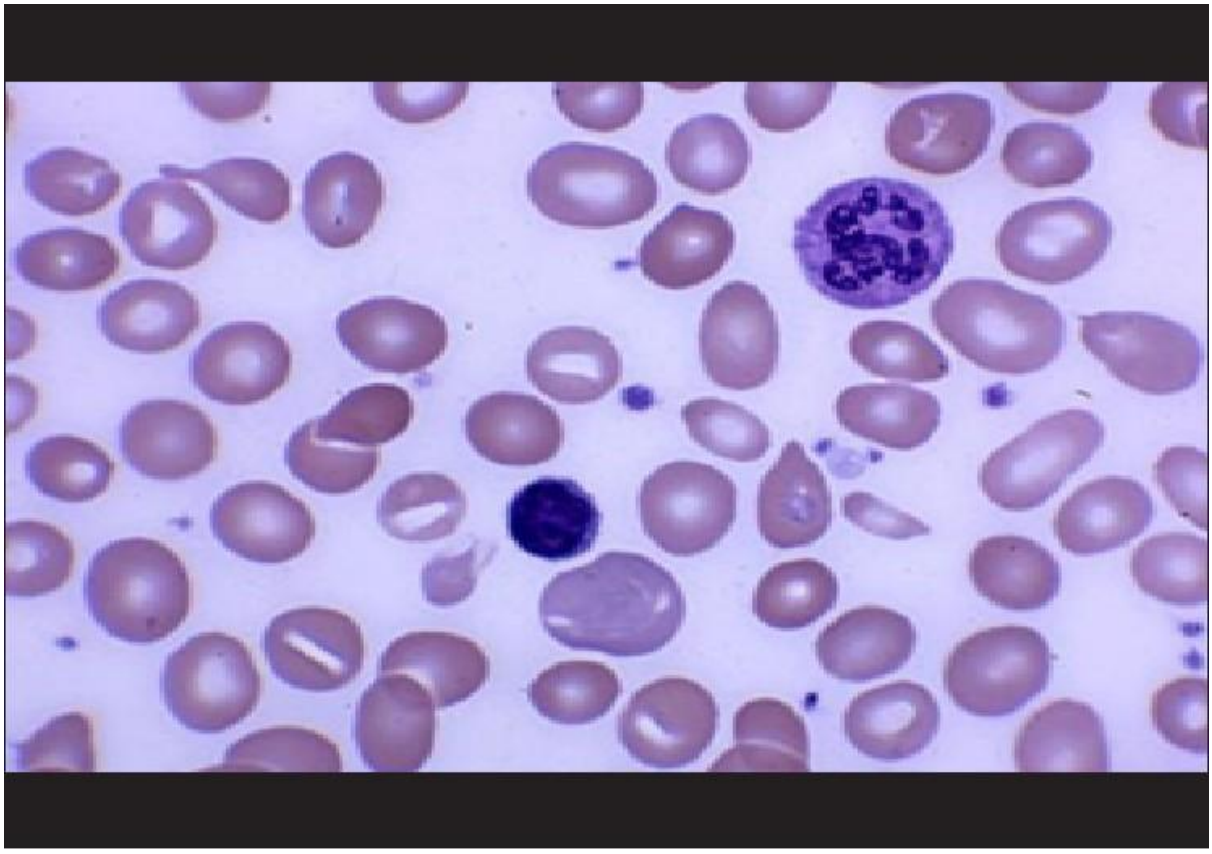
Platelet



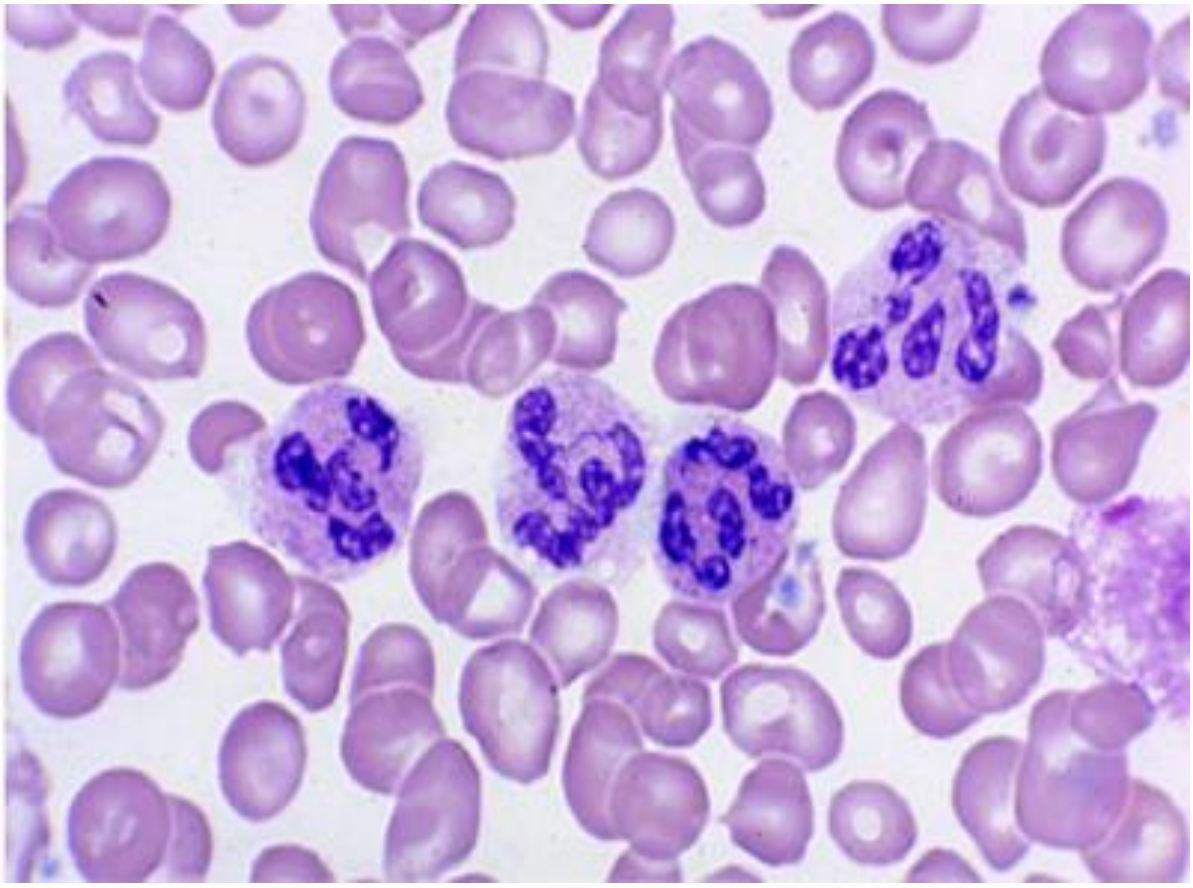
# Hypochromic/Microcytic Anemia
# Iron Deficiency



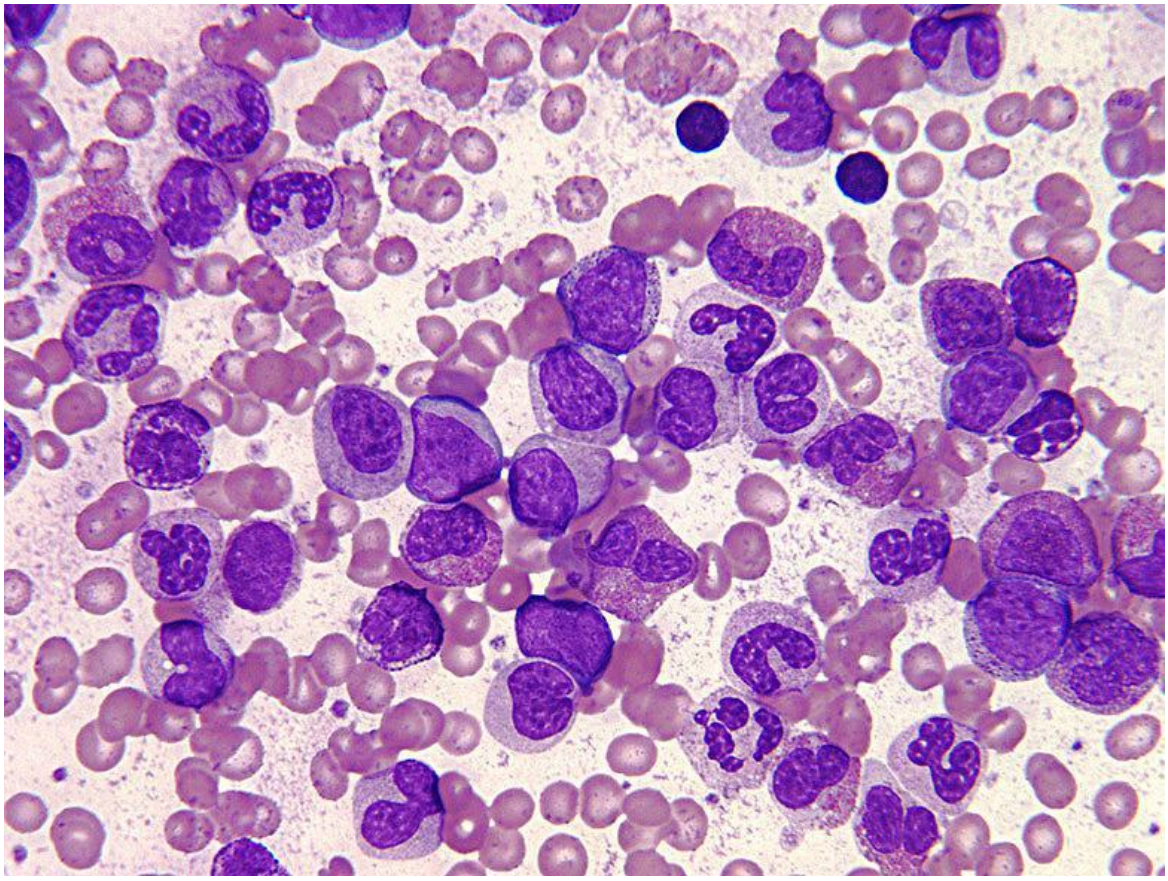
# MACROCYTIC ANEMIA



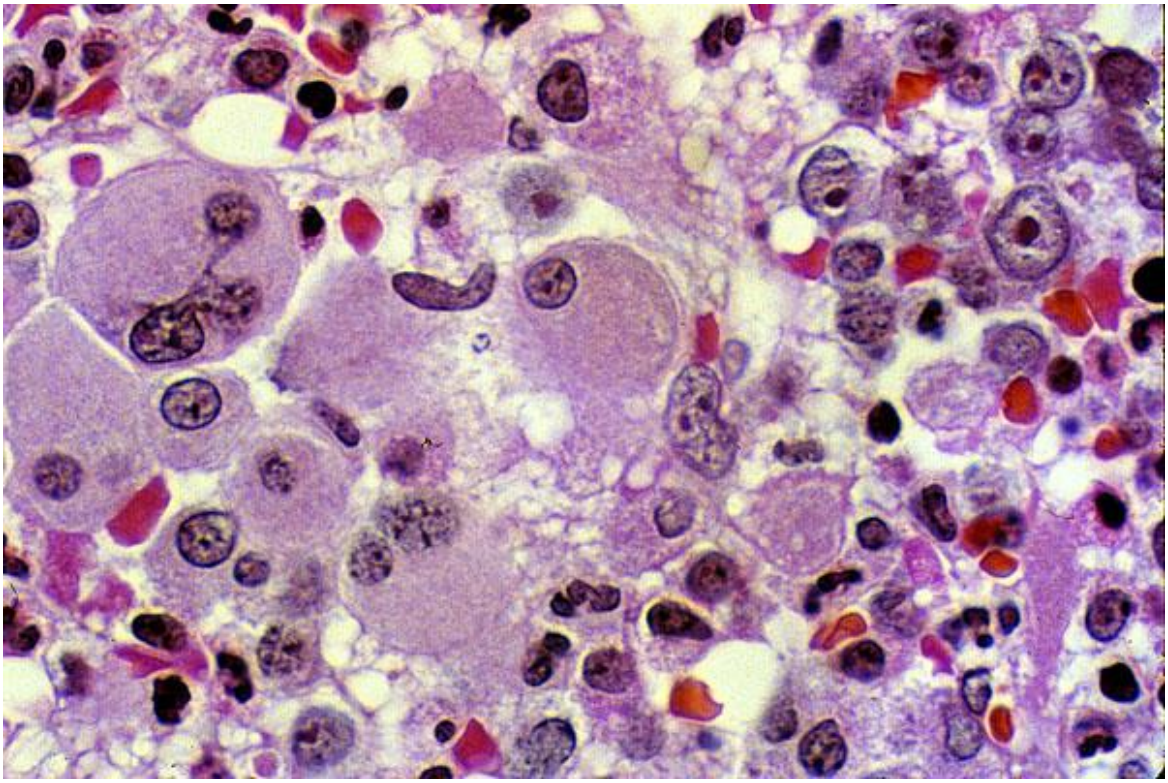
# HYPERSEGMENTED NEUTROPHILS



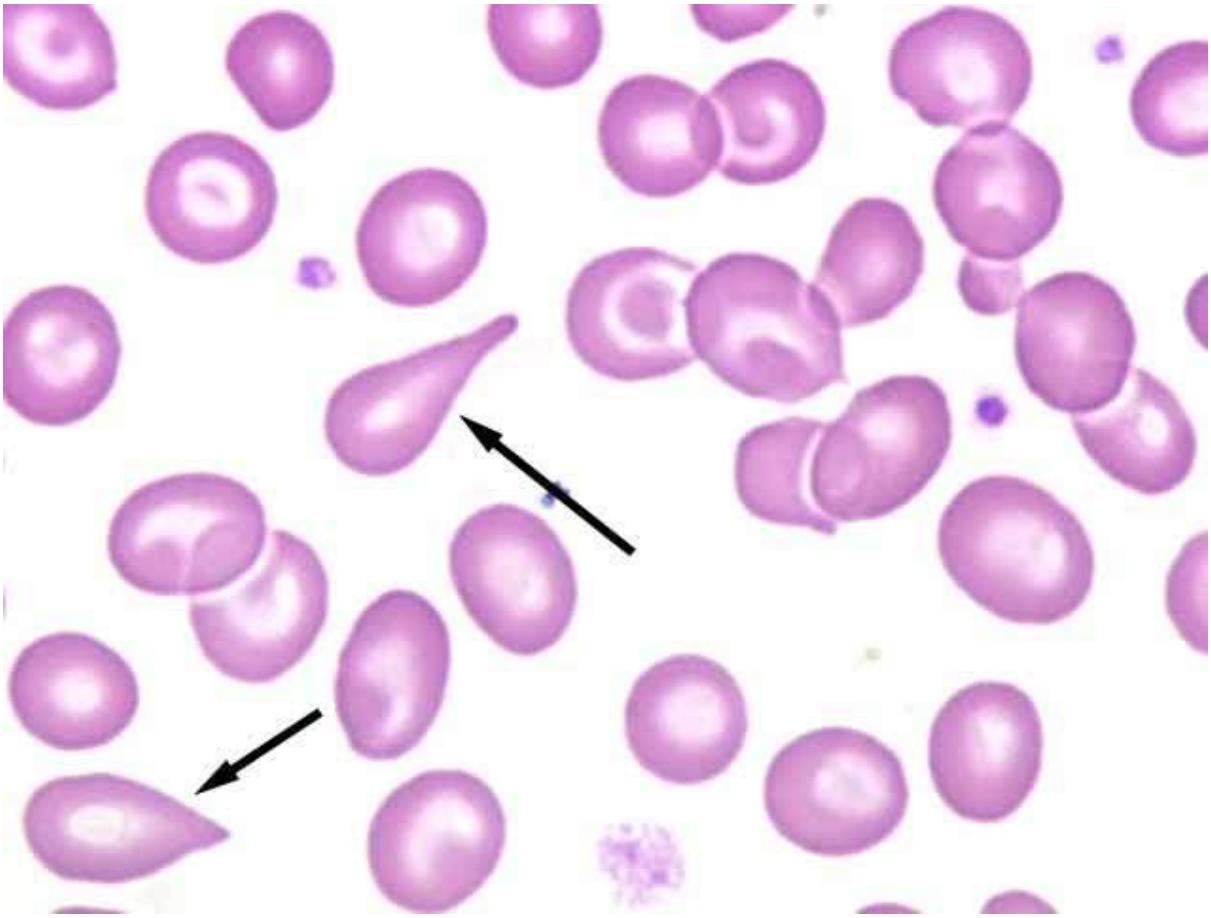
# PERIPHERAL BLOOD PICTURE OF ACUTE MYELOID LEUKEMIA



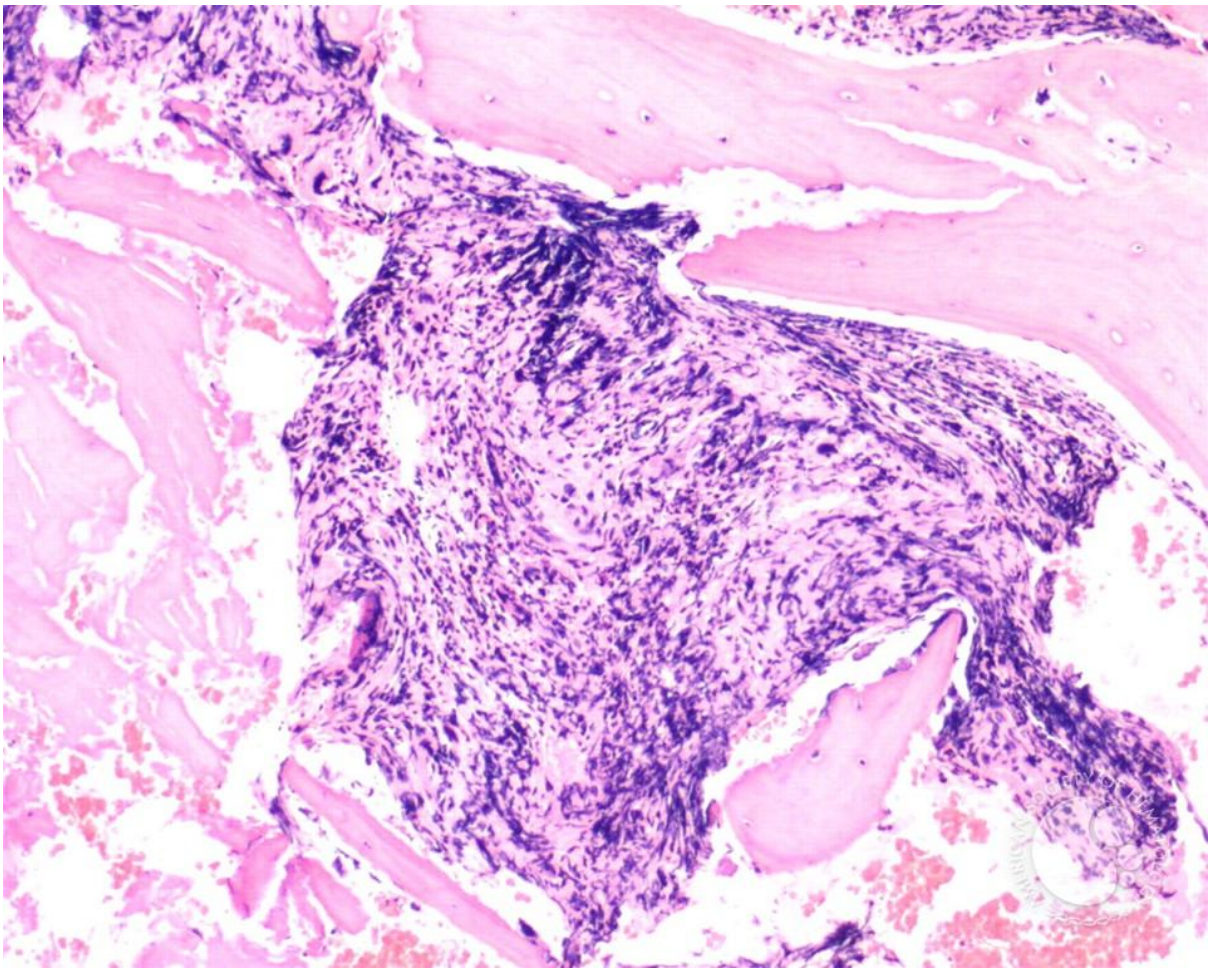
# BONE MARROW PICTURE OF ACUTE MYELOID LEUKEMIA



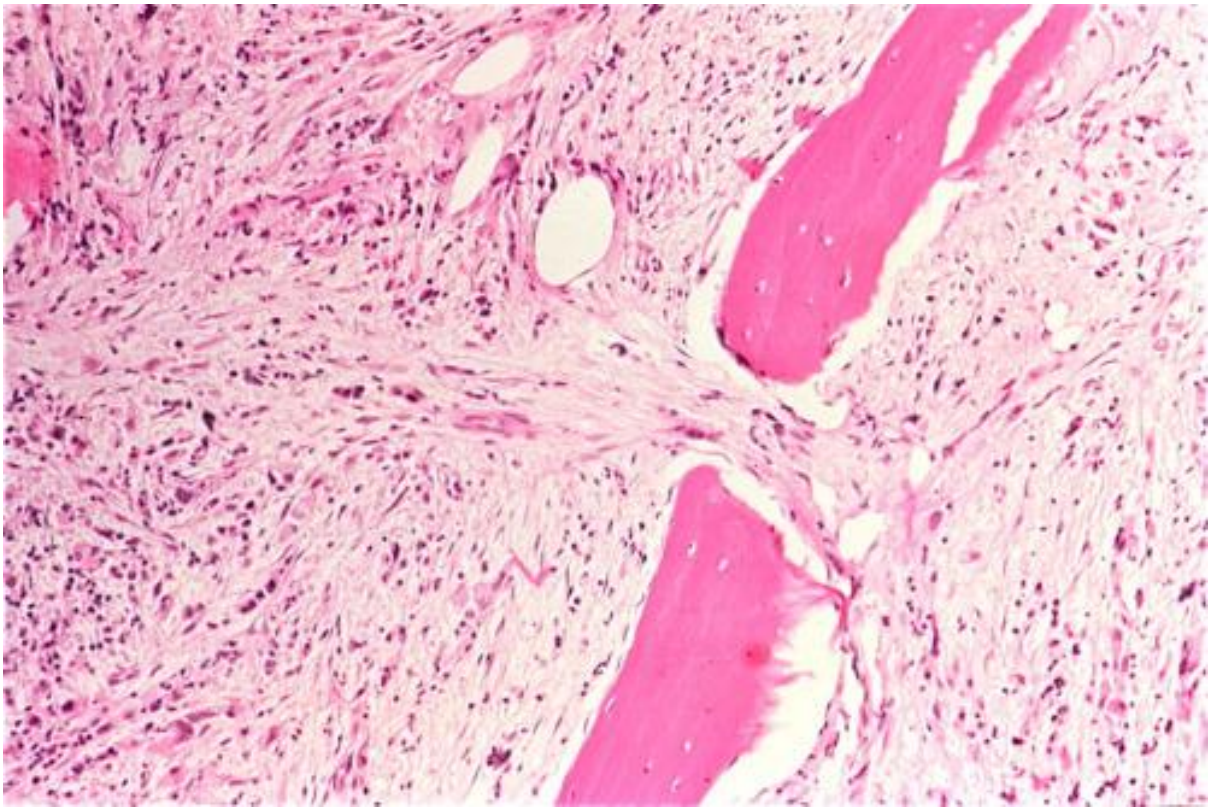
# TEAR DROP CELLS



# BONE MARROW PICTURE IN MYELOFIBROSIS



# BONE MARROW PICTURE IN APLASTIC ANEMIA



**Major Functions of Blood Cells[4]**

RBCs- Delivers oxygen to tissues from lungs and carbon dioxide back from tissues to lungs

WBCs-

Neutrophils- Recognise, ingest and destroy foreign particles & microbes

Eosinophils- Phagocytic, involved in intracellular killing of protozoa and helminths, also involved in allergic reaction

Basophils- Involved in hypersensitivity reactions

Monocytes- Migrates into tissue where they become macrophages, antigen presenting dendritic cells or Kupffer cells and helps in removing microorganisms, apoptotic cells and debris

Lymphocytes- Mediate cellular and humoral immunity

Platelets- Aggregate at site of tissue damage and forms a plug to arrest hemorrage

# HYPERSPLENISM[1]

It is a well known fact that certain patients with splenomegaly due to various diseases develop neutropenia, anemia or thrombocytopenia, and that splenectomy results in improvement of the peripheral blood picture, even back

to normal though usually reversal of granulocytopenia is not sustained. This fact, that the peripheral blood picture may be corrected by splenectomy, led to the concept of hypersplenism.

## Clinical Features

The initial clinical picture varies widely. Manifestations depend on the severity of the anemia, thrombocytopenia or leucopenia. Sometimes splenomegaly is detected as an incidental feature in a patient, who has presented with symptoms of a disorder that is capable of diminishing the levels of all the cellular elements of blood.

The clinical features and simple laboratory findings reflect the underlying disease process. Thus, the presence of splenomegaly calls attention to the possibility of leukemia, myelofibrosis or a congestive cause for splenomegaly. The presence of enlarged lymph nodes supports the possibilities of leukemia, one of the lymphomas, or SLE. The presence of rouleaux formation in the bloodsmear or Bence Jones protein in the urine suggests myeloma. Immature erythrocytes and leukocytes in the blood smear (leukoerythroblastic blood picture) should lead the clinician to consider infiltrative disease of bone marrow (for example, metastatic carcinoma, leukemia or myelofibrosis). The anemia in disorders with pancytopenia is usually normochromic and normocytic, but occasionally it is mildly macrocytic.

## Etiology

**Primary (idiopathic)**

**Secondary:**

Portal hypertension with congestive splenomegaly

Lymphomas

CLL

Hairy cell leukaemia

Infections like Tuberculosis, malaria, kala azar

## Mechanism of hypersplenism[1]

The process involved in lowering of RBC count, is the pooling of red cells within the enlarged spleen. Cytopenia results from greater destruction of cellular elements caused by decreased flow of blood through enlarged and congested cords or due to immune related mechanisms. Radionucleotide studies indicate that passive pooling of red blood cells within the spleen has a greater impact in lowering of red cell count in the blood rather than the accelerated destruction of entrapped red cells.

## Diagnostic criteria for hypersplenism

1. Anemia, leucopenia, thrombocytopenia, either singly or in combination
2. Cellular or hyperplastic bone marrow picture
3. Splenomegaly
4. Marked improvement following splenectomy in peripheral smear

## Blood picture

- Anaemia is usually normocytic and normochromic although they may be spherocytic due to longer transit in enlarged spleen causing loss of surface area.
- Leukopenia is primarily due to accompanying neutropenia, but in severe cases all white cells get reduced.
- Moderate thrombocytopenia can occur with a platelet count of about 100 X $10^9$/L, but occasionally values can drop upto 50 X$10^9$/L.

## Bone marrow[1,4]

Bone marrow either shows normal or increased cellularity or may show infiltration by disease process that is responsible for splenic enlargement.

## Megaloblastic anaemia[1,2]

## PATHOGENESIS OF MEGALOBLASTIC ANAEMIA

Megaloblastic anaemia occurs due to abnormal maturation of hematopoietic cells caused by impaired DNA synthesis. Cobalamine (vitamin B12) and folic acid are two essential vitamins required for DNA biosynthesis. Deficiency of either of them results in what is known as nucleo-cytoplasmic asynchrony. All actively dividing cells will exhibit megaloblastosis; hence changes are evident in the cells of small intestine, buccal mucosa, tongue, uterus, cervix and vagina. In the haematopoietic system this asynchrony results in normal cytoplasmic maturation along with abnormal nuclear maturation resulting in apoptosis, intra-medullary haemolysis, ineffective erythropoeisis, pancytopenia and typical morphological abnormalities in the bone marrow and peripheral smear which are mentioned later.

### Causes of Folic acid deficiency[2]

Nutritional deficiency

Substance abuse, Alcoholism, Poor dietary intake, Overcooked foods

Malabsorption

Celiac disease, Infiltrative bowel disease, Inflammatory bowel disease, Short bowel syndrome

Drugs

Trimethoprim, Methotrexate, Alcohol, Phenytoin

Increased requirements

Pregnancy, Lactation, Exfoliative dermatitis, Chronic haemolysis

**Causes of Vitamin B12 Deficiency[2]**

Gastric abnormalities

Including atrophic gastritis leading to malabsorption of cobalamin, Zollinger – Ellison syndrome, gastric bypass surgeries

Intestinal causes

Includes pancreatitis, radiotherapy, HIV infection, gluten induced enteropathy, Graft versus host disease etc..

Pernicious anemia

Autoimmune metaplastic atrophic gastritis

Malabsorption syndrome

Small bowel disease

Blind loops

Ileal resection or bypass

Crohn's disease

Pancreatitis

Pancreatic insufficiency

Diet

Strict vegetarians

Vegetarian diet during pregnancy

Agents that can affect absorption

Colchicine

PAS

Neomycin

Biguanides

Anticonvulsants

Proton pump inhibitors

Cytotoxic drugs

N2O anesthesia

Alcohol

## Clinical Manifestations of Cobalamin Deficiency[2]

The classic picture of Cobalamine deficiency due to pernicious anemia was that of a prematurely graying, mentally sluggish person with a shiny tongue (atrophic glossitis) and a shuffling broad gait. This classic picture of pernicious anemia is now seen less frequently. It has been replaced by more subtle presentations. Because Cobalmine is required for all rapidly growing cells

including enteric mucosal cells and epithelial cells of the skin, patients with Cobalamine deficiency may complain of glossitis, vaginal atrophy, and malabsorption; they often have diffuse hyper-pigmentation particularly increased pigmentation over knuckles. The patient may have neuro-psychiatric problems consisting of paraesthesiae, numbness, weakness, impaired memory and personality changes. Examination reveals haematologic and neurologic abnormalities. When the anaemia is severe, there may also be thrombocytopaenia and neutropaenia (i.e. pancytopenia). Thrombocytopenia occasionally may be associated with frank mucosal bleeding.

**Neurologic Abnormalities**[1]

The neurologic abnormalities when they occur, presents with subacute paresthesias in upper and lower limbs with loss of position and vibration sense and a progressive spastic and ataxic weakness. Presence of Babinski sign with absent reflexes caused by peripheral neuropathy is classical of this condition. This classical picture of subacute combined degeneration of spinal cord is specific for vitamin B12 deficiency, and is caused by defect in myelin formation due to unknown mechanisms. The myelopathy is symmetrical and tends to be diffuse affecting legs more than the arms with associated spasticity, clonus, paraplegia and even faecal and urinary incontinence. Other neurologic abnormalities seen include loss of memory, optic atrophy, mental changes and dementia.

## Clinical Manifestations of folic acid deficiency[2]

The haematologic manifestations of folate deficiency are similar to those of Cobalamine deficiency but neurologic abnormalities do not occur. Another important difference is the time required for deficiency to develop. Because Cobalamine stores are so large in body in relation to daily intake, a year of inadequate intake or absorption is required before the development of symptoms. On the other hand, symptoms of folate deficiency can occur within a few weeks after intake is diminished. Folate deficiency occurs in patient who abuse alcohol or other drugs and have a very poor dietary intake. Older and depressed patients who live alone and avoid cooking foods that contain folate may become deficient, as can patients with malabsorption syndrome. Increased folate demands occur in patients with chronic severe haemolytic anaemia and pregnancy.

## Hyperhomocysteinaemia

Both Cobalamine and Folic acid are required for metabolism of homocysteine to methionine. As a result, deficiencies in these vitamins can lead to increase in plasma homocysteine levels, which can then lead onto the development of atherosclerosis and venous thrombosis.

## DIAGNOSIS OF MEGALOBLASTIC ANAEMIA[2,9]

The evaluation of suspected Cobalamine or folate deficiency generally proceeds through two stages: Documentation of the presence of the vitamin deficiency and then determination of its cause (e.g. malabsorption, dietary deficiency or Pernicious anemia). The diagnosis of deficiency can most often be established by a combination of the following; mean corpuscular volume (MCV) of RBCs, peripheral blood smear evaluation and bone marrow studies; measurement of the serum B12 and the red blood cell (or serum) folate concentrations and evaluation of specific metabolites (e.g. methylmalonic acid and homocysteine).

An elevation in MCV of erythrocytes is one of the hallmarks of B12 and folate deficiency. The degree of elevation of the MCV is often a clue to the presence of vitamin deficiency. The major haematologic finding is a macro-ovalocytic anaemia (with increased serum bilirubin and LDH levels that reflect the increased RBC breakdown due to inefficient erythropoiesis). The absolute reticulocyte count is normal or even distinctly low. The peripheral blood smear shows macroovalocytes, occasionally megaloblasts and hyper-segmented neutrophils (forming more than 5% of neutrophils) with 5 or more lobes or 1% with 6 or more lobes. Hypersegmentation is the result of an alteration of late granulopoiesis. When the anaemia is severe, there may also be associated thrombocytopaenia and neutropaenia (i.e. pancytopaenia). Bone marrow

aspiration and biopsy reveal a hypercellular marrow with giant metamyelocytes and megaloblastic erythroid hyperplasia.

**Confirming the diagnosis**

If serum folate and cobalamin concentrations are >4 ng/ml and >300 pg/mL respectively, deficiencies of the two vitamins are quite unlikely. If the above two tests are not within range, the next step is evaluation of the metabolites, methylmalonate (MMA) and total homocysteine. If test results are within the normal range for both, deficiency of both these vitamins can be ruled out.

**Treatment**[1]

Folic acid deficiency — Standard dosing of oral folic acid is 1 to 5 mg orally daily for about four months or until complete haematologic recovery occurs. Vitamin B12 deficiency must be ruled out, and treated if present, before giving folic acid to a patient, since administration of folic acid alone can lead on to worsening of neurologic complications of untreated vitamin B12 deficiency.

Cobalamine deficiency — For patients with permanently impaired ability to absorb vitamin B12 from food (eg- pernicious anemia, total gastrectomy), life-long treatment is necessary. Intially parenteral vitamin B12 is preferred over oral therapy. Maintenance therapy with oral therapy is also possible.

## Aplastic Anaemia[3, 23]

Aplastic anaemia (AA) is defined by the presence of pancytopaenia with hypocellular marrow in which normal haemopoietic marrow is replaced by fat cells. It shows a biphasic distribution with two peaks, one in the age group of 15-25 and the other peak after 60 years. It is a life-threatening disorder, which if left untreated, is associated with a very high mortality rate. A rare disorder which is characterized by diminished or absent hematopoietic precursors in the bone marrow chiefly due to failure of pluripotent stem cells resulting in hypoplasia of bone marrow and pancytopenia. Stem cell failure can be congenital (eg- Fanconi's anemia) or more often acquired**.** Bone marrow failure usually occurs due to severe damage to hematopoietic cell compartment. The cells which bear the CD34 antigen, a marker of early hematopoietic cell, are greatly decreased.

### Causes[14]

Congenital

Fanconi anemia — There are numerous causes for congenital aplastic anemia. The most common is Fanconi's anemia,a familial condition characterized by pancytopenia, macrocytic anemia and congenital malformations.

Dyskeratosis Congenita

Shwachman- Diamond Syndrome

Acquired

Cytotoxic drugs and radiation

Drugs

Anticonvulsants

- Carbamazepine
- Phenacemide
- Hydantoins

Immunosuppresives

- Azathioprine

Antibiotics

- Sulfonamides
- Chloramphenicol

Antirheumatics

- Phenylbutazone,
- Indomethacin
- Gold
- Penicillamine

Anti-Thyroid Medications

- Methimazole
- Propylthiouracil

Toxic chemicals

- Benzene toluene solvents
- Glue vapors

Insecticides

- DDT
- Organophosphorous compounds
- Organocarbamates

Viral infections

- Epstein-Barr virus
- Seronegative hepatitis
- Human immunodeficiency virus
- Other herpes viruses

Immune disorders

- Eosinophilic fasciitis
- Systemic lupus erythematosus
- Graft versus host disease

Miscellaneous

- Radiation
- Thymoma
- Pregnancy
- Anorexia nervosa

## Clinical features[11]

They usually present with easy fatigability and cardiopulmonary complications. There may be recurrent infections due to neutropenia, and bleeding can occur following development of thrombocytopenia. Bacterial, viral and fungal infections can occur following aplasia. Pallor and petechiae are the usual clinical manifestations. Hepatomegaly and splenomegaly usually does not accompany.

## Diagnosis

- Peripheral blood picture will show pancytopenia, low reticulocyte count and often macrocytosis.
- Bone marrow examination will reveal hypocellular marrow with a decrease in all the elements; the marrow space will be composed mainly of fat cells and marrow stroma. Residual hematopoietic cells will be morphologically normal and hematopoiesis will not be megaloblastic.

## Treatment[1]

It invoves blood product support and control of infection. If the age of patient is less than 30 years, allogenic bone marrow transplantation may be considered where they have 75-90% long term cure chance. In elderly use of immunosuppressives like ciclosporin and antithymocyte globulin gives a 5 year survival of 75%.

# Multiple Myeloma[1,3]

It is characterised by neoplastic proliferation of immunoglobulin-secreting plasma cells of a single clone. Most patients present with organ dysfunction, symptoms or signs related to the infiltration of plasmacells into the bone or other organs thereby resulting in bony pain or fractures, kidney damage, anemia, hypercalcemia, neurological symptoms, hyperviscosity manifestations and clotting abnormalities from excess light chains.

## Clinical features

Back ache is the most prevalent symptom in myeloma which is seen in about 70% of patients. This is followed by susceptibility to infections, most common being infections of lung and renal tissue. Most common pathogens implicated *are Staphylococcus aureus, Streptococcus pneumonia* and *Klebsiella pneumoniae* in lungs and *Escherichia coli* in genitourinary tract. Anemia, renal failure or proteinuria, fatigue, and hypercalcemia are other common manifestations. Less common presentations include spinal cord compression, deep vein thrombosis and polyneuropathies.

## Specific investigations

Classic triad[3] of multiple myeloma is lytic bone lesions, marrow plasmacytosis(>10%) and a serum and/or urine M component.

- Blood and urinary protein electrophoresis
- Blood and urine immunoelectrophoresis
- Bone marrow aspiration and trephine
- Plasma immunoglobulins
- Serum light chain assay
- MRI spine
- Serum beta 2 microglobulin (provide an idea regarding prognosis)

**Diagnostic Criteria( all 3 must be met)**

- Presence of 10% or more clonal bone marrow plasma cells or a biopsy proven plasmacytoma
- Presence of M-protein in serum and/or urine
- Presence of a related organ or tissue impairment that can be attributed to plasma cell proliferative disorder (anemia, renal insufficiency, increased serum calcium and lytic bone lesions)

**Differential Diagnosis**

- Monoclonal Gammopathy Of Undetermined Significance (MGUS)
- AL Amyloidosis
- Smoldering Multiple Myeloma (SMM)
- Solitary Plasmacytoma
- Waldenstrom Macroglobulinemia
- POEMS Syndrome
- Metastatic Carcinoma.

Presence of paraproteins in blood will cause background basophilic staining and increased clustering of RBCs (rouleaux formation). Lytic bone lesions may be seen in any of the bones. The following distribution was found in a large case series study with vertebral column affected in 66%, ribs in 44% cases, skull in 41%, followed by pelvis, femur, clavicle and scapula.

## Management[1]

Asymptomatic- No treatment

Analgesics for bony pains

High fluid intake

Bisphosphonates for hypercalcemia

Allopurinol to prevent urate nephropathy

Plasmapheresis for hyperviscosity

In transplant candidates- Newer agents like bortezomib or lenalidomide combined with pulsed glucocorticoids

Non transplant candidates- intermittent pulses of an alkylating agent like melphalan with prednisone.

# PAROXYSMAL NOCTURNAL HEMOGLOBINURIA[1]

Lewis and Dacie, in 1967, suggested that "PNH represents a somatic mutation in the hematopoietic stem cell which was already damaged during an aplastic episode". Triad in PNH include hemolysis, pancytopenia and tendency for venous thrombosis. Patient seeks doctor's advice following passage of blood instead of urine. Some others present with recurrent attacks of abdominal pain. When thrombosis occurs in hepatic veins it cause hepatomegaly with ascites which may be suspected as PNH in the absence of liver disease. An acquired mutation in the *PIG-A* gene of haematopoietic stem cells, results in a clone of progeny without glycosylphosphatidylinositol-linked cell surface membrane proteins[22]. PNH cells are detected by expression of CD55 or CD59 on granulocytes detected by flow cytometry[23]. Definitive diagnosis of PNH must be made on demonstration of RBCs showing increased susceptibility to compliment C due to deficiency of CD 59 and CD55, proteins that protect RBCs from activated C. Gold standard is flow cytometry while other tests used are sucrose hemolysis test and Ham test. Thrombosis is one among the life threatening complications of PNH.

Treatment of PNH includes supportive therapies like transfusion, iron and folic acid supplementation, IV eculizumab every 14 days. Definitive cure is accomplished by allogenic bone marrow transplantation.

# MYELODYSPLASIA[1, 23]

They are a heterogeneous group of haematologic disorders characterised by cytopenias with a dysmorphic and usually cellular bone marrow resulting in ineffective blood cell production.

## WHO Classification

Refractory cytopenias with unilineage dysplasia

Refractory anemia with ringed sideroblasts

Refractory cytopenias with multilineage dysplasia

Refractory anemia with excess of blasts

MDS associated with isolated Del(5q)

Childhood MDS

Unclassifiable MDS

## Epidemiology

Idiopathic MDS is a disease of the old age with a mean age of onset after 70 years and a slightly increased male incidence.

## Etiology and pathophysiology

They are frequently linked to environment exposures to radiation and benzene. Secondary myelodysplastic syndromes occur as a late toxicity to cancer therapy. Impaired cell proliferation and differentiation can occur with MDS. Cytogenetic abnormalities are found in almost half the number of patients with MDS.

Pathophysiology – They result from multiple genetic lesions, loss of tumour suppressor genes, activation of oncogene or their mutations, inefficient erythropoiesis and deranged iron metabolism are some of the usual functional consequences of the genetic alterations in myelodysplasia.

## Clinical features

Anaemia is the predominant feature in the early course. Most patients present with complaints of gradual onset of fatigue, weakness, dyspnoea and pallor, but at least half of the patients are asymptomatic and MDS is discovered only incidentally on routine examination of blood. The physical examination is remarkable for signs of anemia with about 20% of patients having splenomegaly. Some unusual skin lesions like febrile neutrophilic dermatosis (Sweet's syndrome) have been linked with myelodysplasia.

## Laboratory studies

### Blood

Anaemia is present in the most of the cases, either alone or a part of pancytopenias. Presence of macrocytes in peripheral smear is common and the smear may be dimorphic in nature. Thrombocytes are large and are hypogranulated. Neutrophils may have hyposegmented, ringed or abnormally segmented nuclei. Amount of circulating myeloblasts usually correlate with number of blasts in marrow and is important in classification and prognosis.

### Bone marrow

Marrow is usually normal or hypercellular, but in few (20%) cases it may be sufficiently hypocellular to get confused with aplasia. There is no single characteristic feature of marrow morphology that distinguishes myelodysplasia from other causes. Dyserythropoietic changes and ringed sideroblasts in the erythroid lineage; hypogranulation and decreased segmentation of granulocytic precursors, with an increase in number of myeloblasts; and megakaryocytes showing decreased numbers of disorganized nuclei are some of them.

### Treatment

Only stem cell transplantation offers cure. However, multiple new drugs have been approved for use in MDS. Supportive care described for aplastic anemia applies to myelodysplasia[23]. Despite improvements in drug therapy, patients will be anemic for many years and blood transfusion should be administered along with iron chelation to prevent secondary haemochromatosis.

# Myelofibrosis[1,2]

Primary myelofibrosis (PMF), previously called chronic idiopathic myelofibrosis (CIMF) also called as agnogenic myeloid metaplasia[12], is one among the chronic myeloproliferative disorders which is characterized by proliferation of myeloid cells with variable morphologic maturity, bone marrow fibrosis, leukoerythroblastic blood picture and extramedullary haematopoiesis. Acute myelofibrosis has been applied to clinical picture seen in AML M7.

## EPIDEMIOLOGY

- Least frequent among the chronic myeloproliferative disorders.
- Occurs mainly in middleaged and elderly.

## CLINICAL PRESENTATION

Most patients present after 50 years of age with weight loss, fatigue and night sweats among which the most common presenting symptom is fatigue. Hepatomegaly and massive spleenomegaly can occur due to extra medullary haematopoesis associated with primary myelofibrosis along with painful splenic infarcts.

Splenomegaly, often marked, is the hallmark of primary myelofibrosis. Palpable hepatomegaly is present in 40 to 70% of patients. Portal

hypertension may develop as a result of increased splanchnic blood flow due to splenomegaly and/or intrahepatic obstruction associated with extramedullary hematopoiesis.

Other sites of extramedullary haematopoeisis

· Lymph nodes

· Vertebral column (especially thoracic vertebrae)

· Genitourinary system

· Retroperitoneum

· Lungs and pleural cavity

Osteosclerosis of bone may occur following primary myelofibrosis .Radiographic appearance of mottling may be seen in primary myelofibrosis.

## LAB FINDINGS[12]

Anaemia

- Autoimmune hemolysis

- Ineffective erythropoiesis associated with extramedullary sites of RBC production

- Decrease in medullary erythropoietic sites

- Sequestration of RBCs in the spleen and destruction of circulating RBCs

- Bleeding caused by thrombocytopenia or other complications like varices resulting from portal vein thrombosis

- Influence of thrombopoietin receptor (Mpl) mutations

Thrombocytosis or thrombocytopenia can occur. Leucocytosis or leucopenia can occur.

Bone marrow aspiration will give a dry tap. If there is any aspirate, that will show neutrophilic and megakaryocytic hyperplasia. Bone marrow biopsy is necessary to demonstrate fibrosis.

Diagnosis of PMF should be entertained only if all of the following features are present at the time of initial detection

- Nucleated RBCs in peripheral blood
- Tear drop RBCs in peripheral blood
- Premature WBCs in the peripheral blood
- Splenomegaly

2008 WHO criteria include a combination of following findings [24]

- Presence of megakaryocyte proliferation and atypia, usually accompanied by reticulin
- WHO criteria for Polycythemia Vera, Chronic Myeloid Leukemia, Myelodysplastic Syndrome or other myeloid neoplasms are not satisfied
- Demonstration of clonal markers ( JAK2 or MPL)
- Leukoerythroblastosis
- Palpable spleen

- Anemia
- Increased serum LDH levels

Median survival is 4 years from the time of diagnosis and the treatment is directed at the control of symptoms like transfusion for anemia. Folic acid should be supplemented to avoid deficiency. Hydroxycarbamide is used to control splenic size, WBC count and systemic features. Splenectomy may be contemplated if the spleen is grossly enlarged or symptomatic pancytopenia secondary to hypersplenism develops. Bone marrow transplantation may be tried in young individuals.

**Metastatic carcinoma**

Patients with carcinoma usually have anemia, with or without associated cytopenias.

1. D**irect toxicity of malignancy**

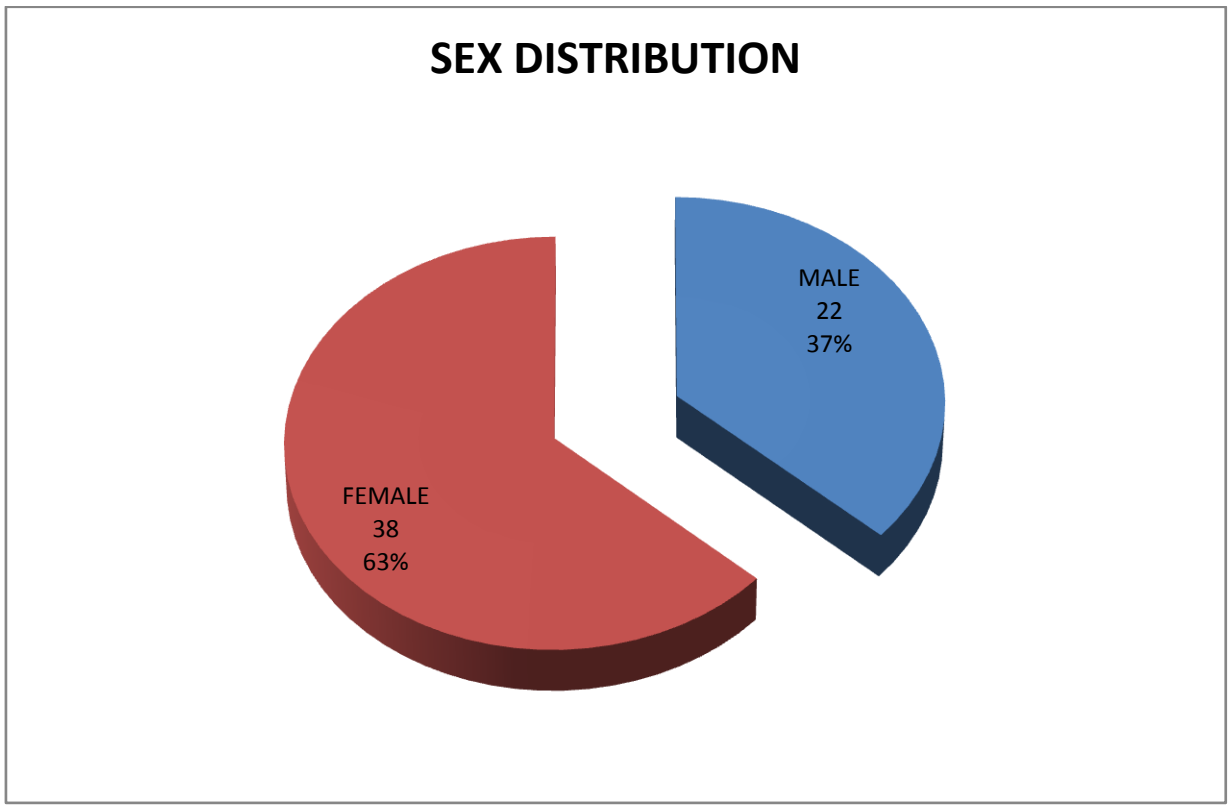
Acute leukemias can directly cause suppression of normal erythropoiesis in marrow, thus resulting in anemia due to marrow failure. As in myelodysplasia, anemia caused by acute leukemia is frequently macrocytic and have a reduced reticulocyte count.

2. **Indirectly resulting from malignancy**

Autoimmune hemolytic anemia are seen in patients with chronic lymphocytic leukemia whereas microangiopathic hemolytic anemia is commonly seen in gastric cancer which also occurs in carcinomas invoving breast and lungs. Another common form of anemia seen in cancer patients is anemia of chronic disease. Here the marrow is normocellular, with a normal myeloid erythroid ratio and an increase in amount of storage iron in histiocytes.

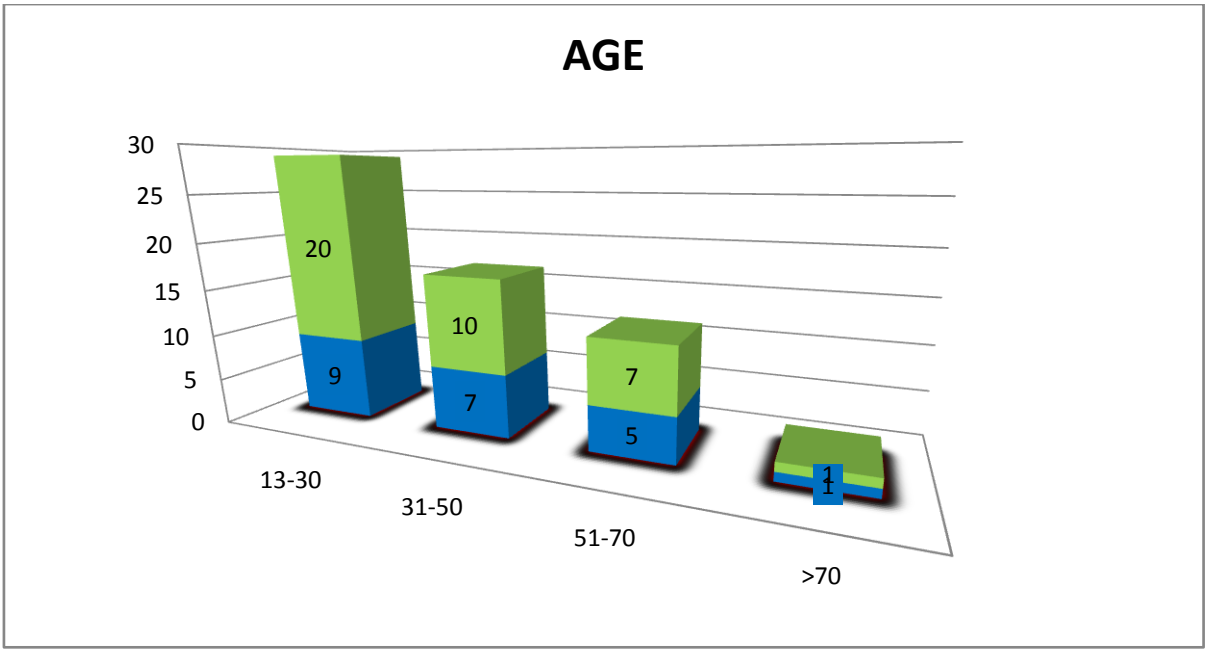
# RESULTS

# RESULTS




| SEX DISTRIBUTION | | |
|---|---|---|
| **SEX** | **COUNT** | **PERCENTAGE** |
| MALE | 22 | 37% |
| FEMALE | 38 | 63% |

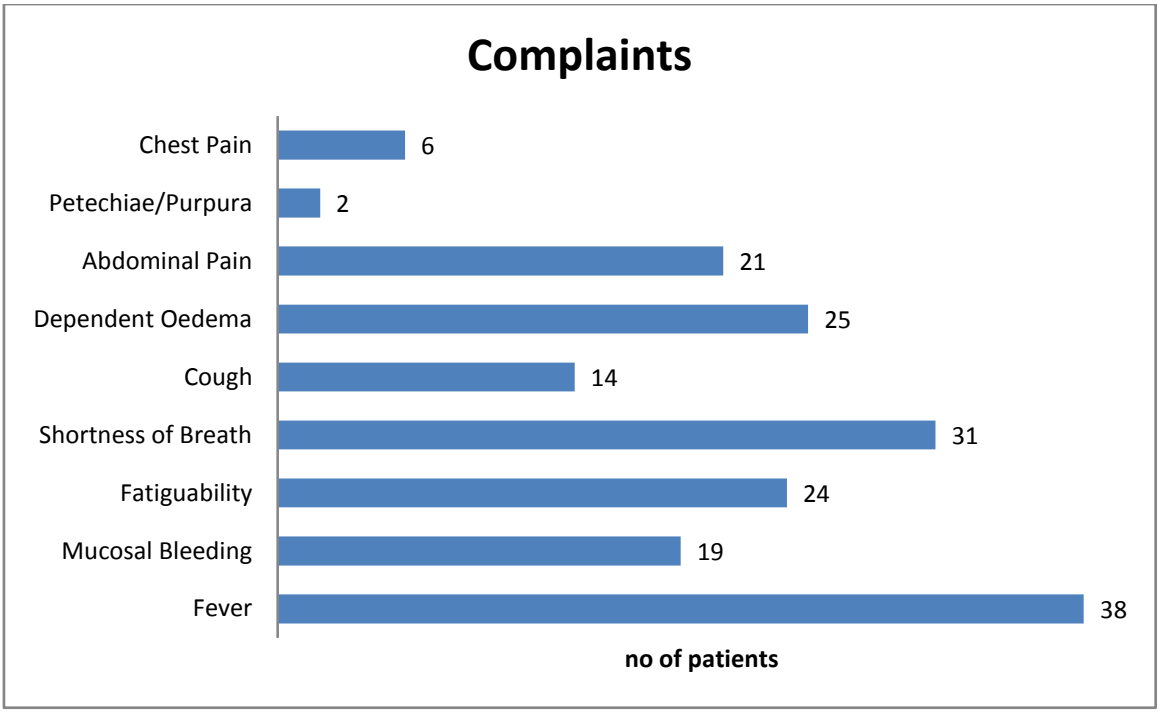
Females formed majority of patients accounting for 63% while men were only 33% of the patients who presented with pancytopenia.




| AGE DISTRIBUTION | | | |
|---|---|---|---|
| **AGE RANGE** | **MALE** | **FEMALE** | **PERCENTAGE** |
| 13-30 | 9 | 20 | 48.33% |
| 31-50 | 7 | 10 | 28.33% |
| 51-70 | 5 | 7 | 20% |
| >70 | 1 | 1 | 3.33% |
| TOTAL | 22 | 38 | 100% |

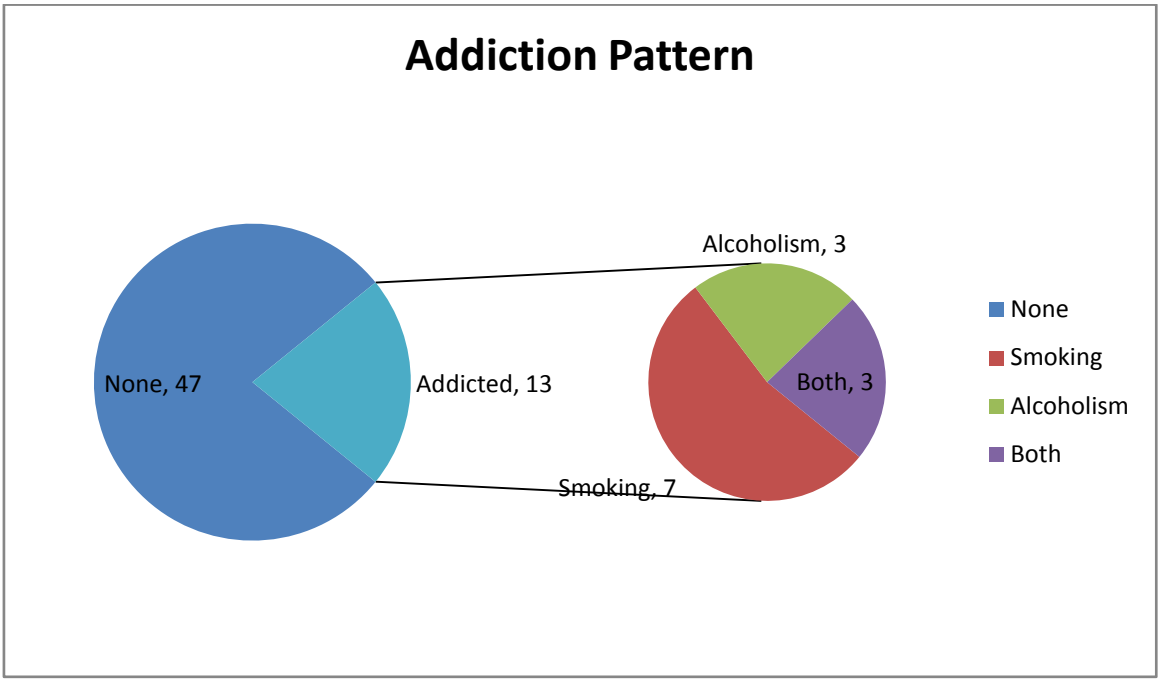
In this study, majority of patients belonged to the age range of 13-30 accounting for 48.33% followed by middle aged people in the 31-50 age range accounting for 28.33% of the studied population.

Average age of patients was found to be 38 with a standard deviation of 18.30. Oldest was an 86 year old male and youngest was a 13 year old boy.



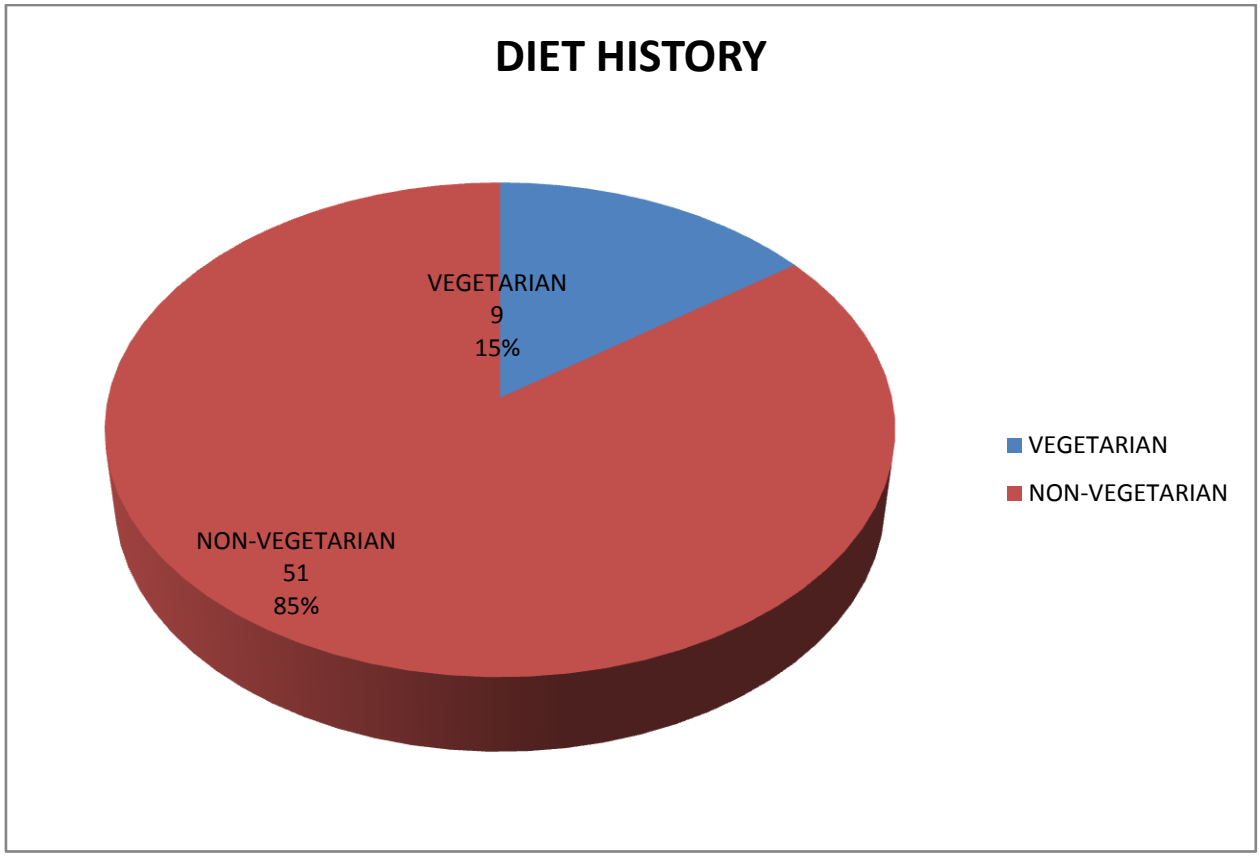

| CHIEF PRESENTING COMPLAINTS | | |
|---|---|---|
| **TYPE** | **COUNT** | **PERCENTAGE** |
| Fever | 38 | 63.33% |
| Mucosal Bleeding | 19 | 31.67% |
| Fatiguability | 24 | 40% |
| Shortness of Breath | 31 | 51.67% |
| Cough | 14 | 23.33% |
| Dependent Oedema | 25 | 41.67% |
| Abdominal Pain | 21 | 35% |
| Petechiae/Purpura | 2 | 3.33% |
| Chest Pain | 6 | 10% |

Chief presenting complaint among those presented with pancytopenia was fever (63.33%) followed by breathlessness (51.67%) and dependant oedema (41.67%).

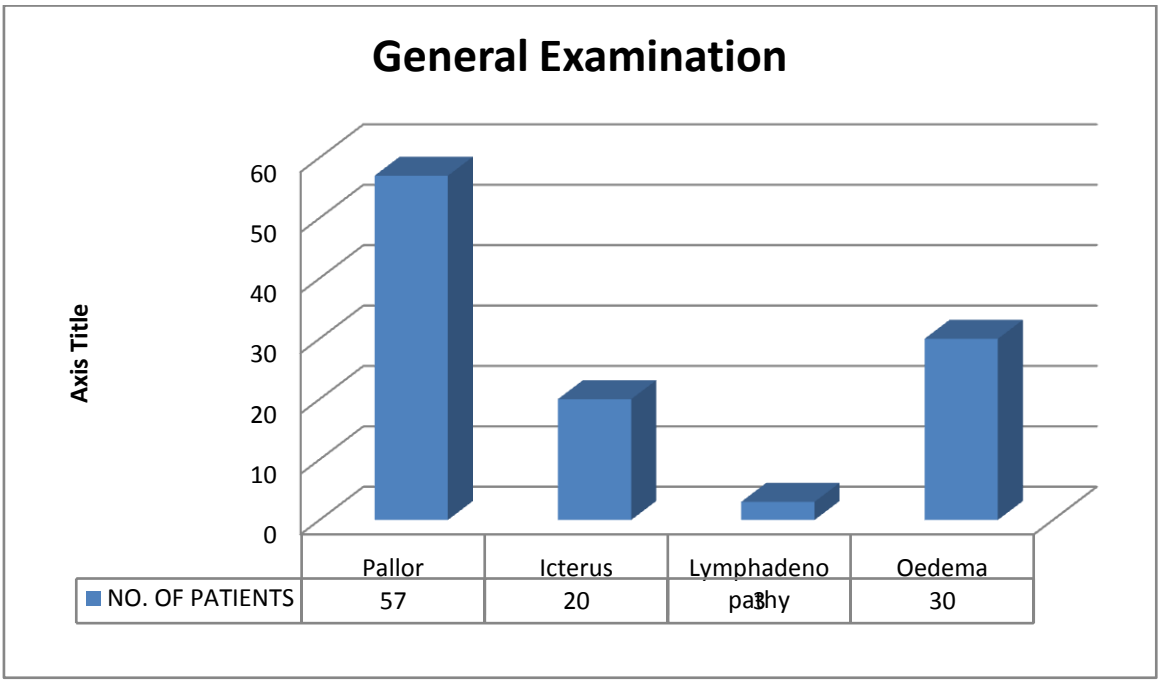



| ADDICTION PATTERN | | |
|---|---|---|
| **ADDICTED TO** | **NO OF PATIENTS** | **PERCENTAGE** |
| None | 47 | 78.33% |
| Smoking | 7 | 11.67% |
| Alcoholism | 3 | 5% |
| Both | 3 | 5% |

About 78% of studied population were free from addiction to either smoking or alcohol consumption. Among those who had a risk behaviour smoking was prevailing(11.67%) with 5% of total study group having both smoking and alcohol consumption as a risk factor.

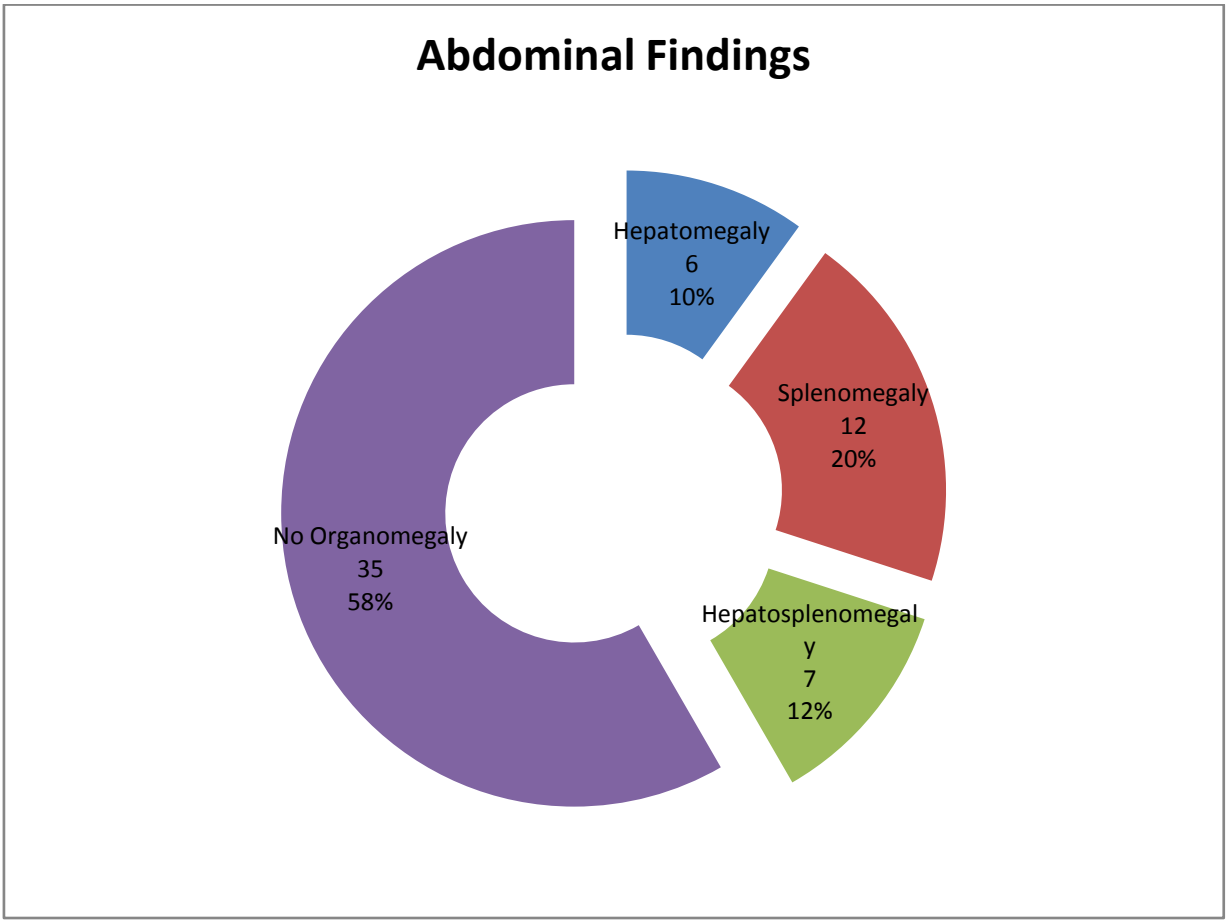



85% of pancytopenia patients were found to be nonvegetarians while rest 15% were found to be vegetarians.



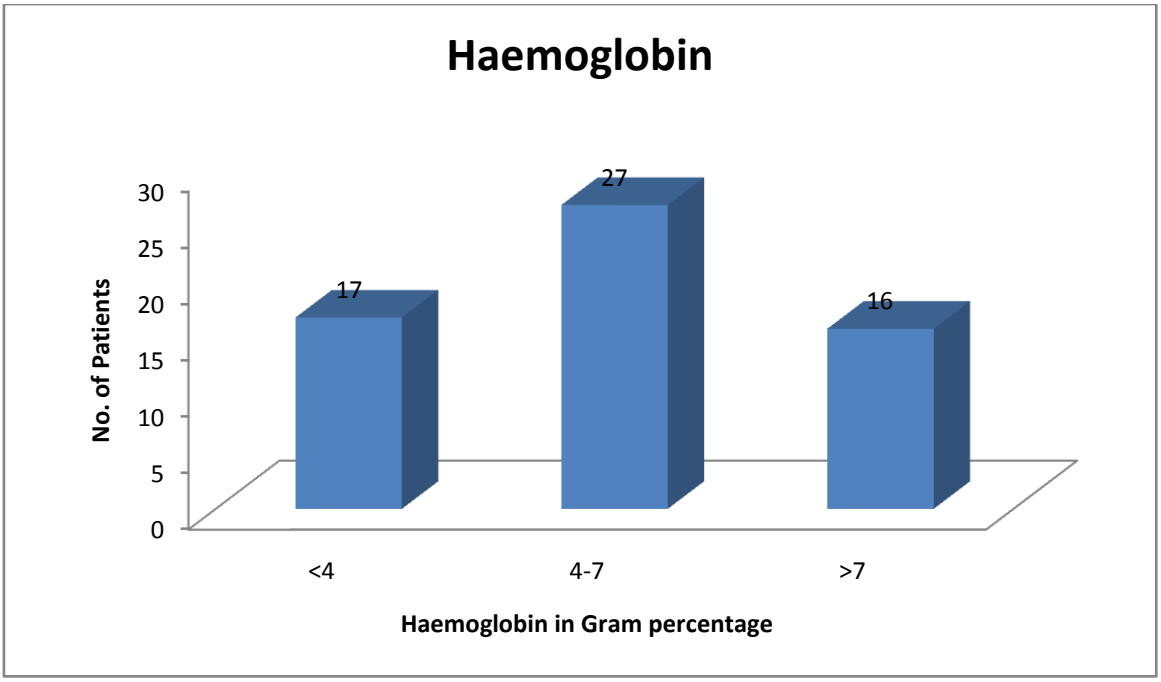

| GENERAL EXAMINATION | | |
|---|---|---|
| | **NO. OF PATIENTS** | **PERCENTAGE** |
| Pallor | 57 | 95% |
| Icterus | 20 | 33.33% |
| Lymphadenopathy | 3 | 5% |
| Oedema | 30 | 50% |

95% of patients who had pancytopenia were appreciated to have clinically significant pallor while 50% had pedal oedema. 33% had clinical evidence of jaundice while 5% had generalised lymphadenopathy.



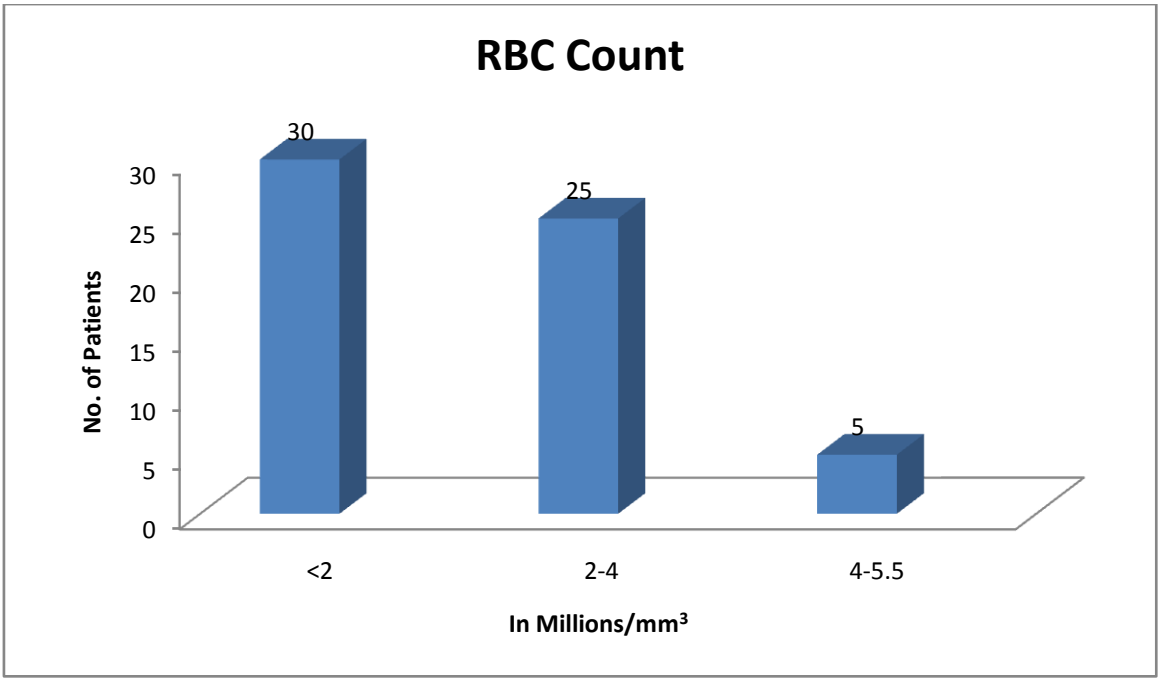

| Abdominal Findings | | |
|---|---|---|
| | **No of Patients** | **PERCENTAGE** |
| Hepatomegaly | 6 | 10% |
| Splenomegaly | 12 | 20% |
| Hepatosplenomegaly | 7 | 11.67% |
| No Organomegaly | 35 | 58.33% |

About 32% of pancytopenia patients had splenic enlargement, 22% had hepatomegaly while 12% had combined hepatosplenomegaly.



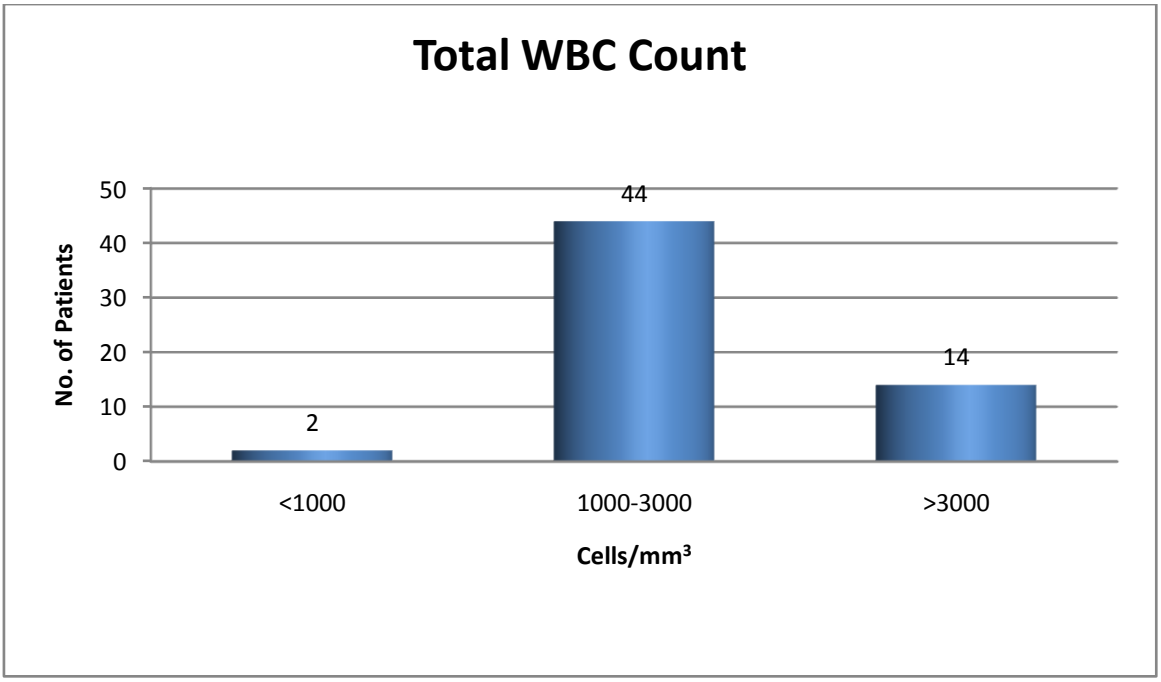

| Haemoglobin in Gram % | No. of Patients | Percentage |
|---|---|---|
| <4 | 17 | 28.33% |
| 4-7 | 27 | 45% |
| >7 | 16 | 26.67% |

45% of patients were found to have moderate anemia, 28.33% had severe anemia and 26.67% had minimal anemia. Average haemoglobin of study population was 5.74+/-2.17. Highest haemoglobin recorded was 9.9gm% while lowest was found to be 2.3gm%.



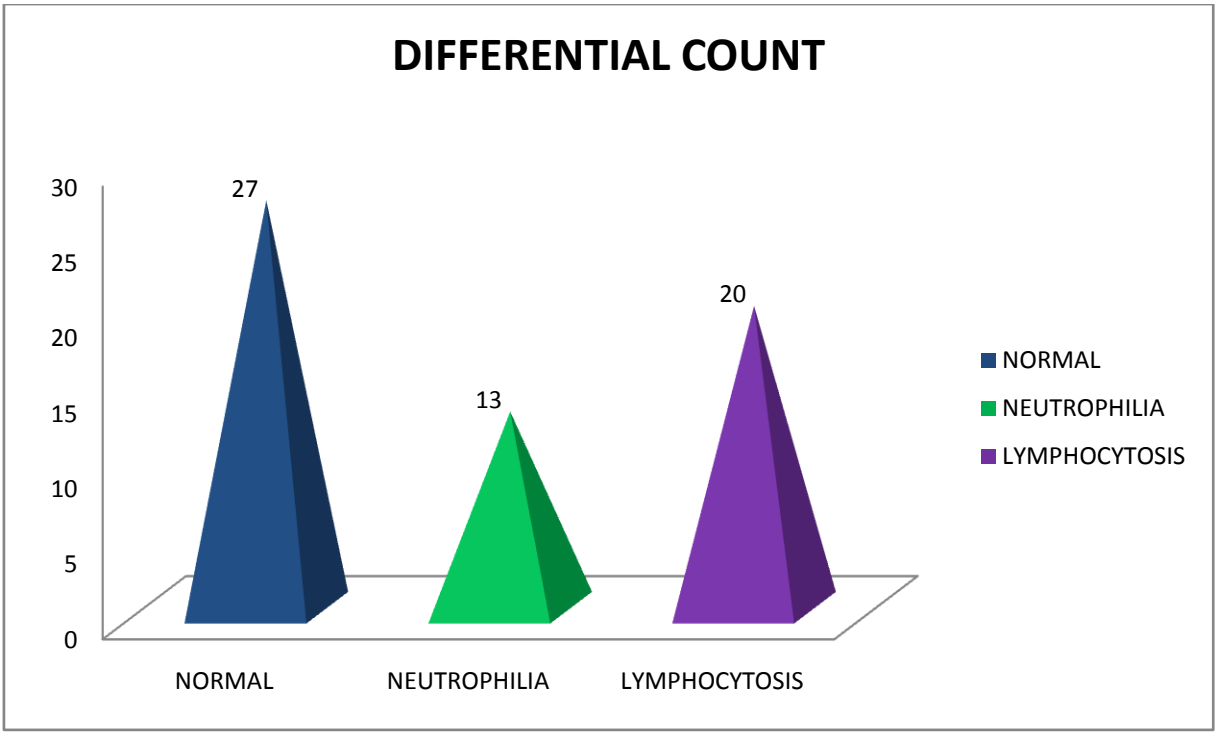

| RBC COUNT | | |
|---|---|---|
| **IN MILLIONS/mm$^3$** | **NO. OF PATIENTS** | **PERCENTAGE** |
| <2 | 30 | 50% |
| 2-4 | 25 | 41.67% |
| 4-5.5 | 5 | 8.33% |

Mean RBC count was found to be 2.16 million/mm$^3$ with a standard deviation of 0.93 million/mm$^3$. Majority of patients having RBC count less than 2million cells/mm$^3$ and 92% had RBC count less than 4 million cells/mm$^3$.



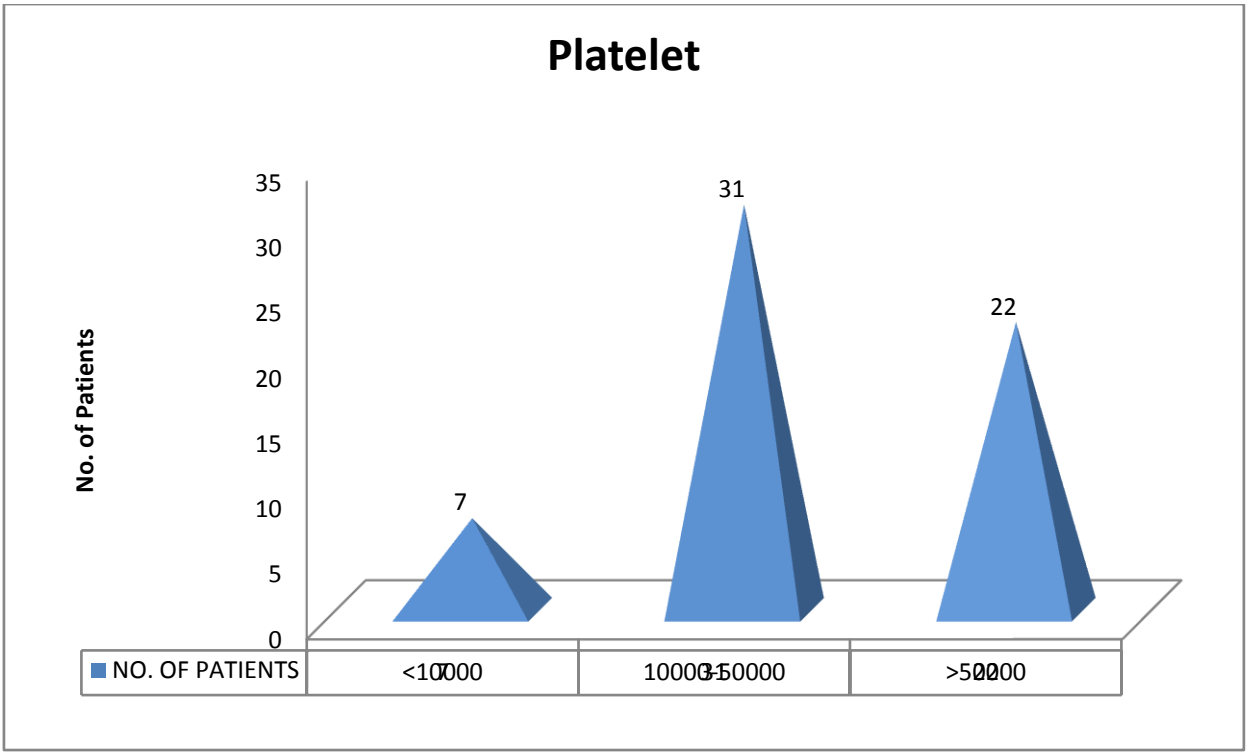

| Total WBC Count | | |
|---|---|---|
| **CELLS/mm$^3$** | **NO. OF PATIENTS** | **PERCENTAGE** |
| <1000 | 2 | 3.33% |
| 1000-3000 | 44 | 73.33% |
| >3000 | 14 | 23.33% |

73% patients presented with total WBC count between 1000 and 3000 cells/mm$^3$, while 2 patients (3.33%) had a very low WBC count of <1000cells/mm$^3$. Average WBC count was found to be 2432+/- 799 cells/mm$^3$.




| DIFFERENTIAL COUNT | | |
|---|---|---|
| **TYPE** | **NO. OF PATIENTS** | **PERCENTAGE** |
| NORMAL | 27 | 45% |
| NEUTROPHILIA | 13 | 21.67% |
| LYMPHOCYTOSIS | 20 | 33.33% |

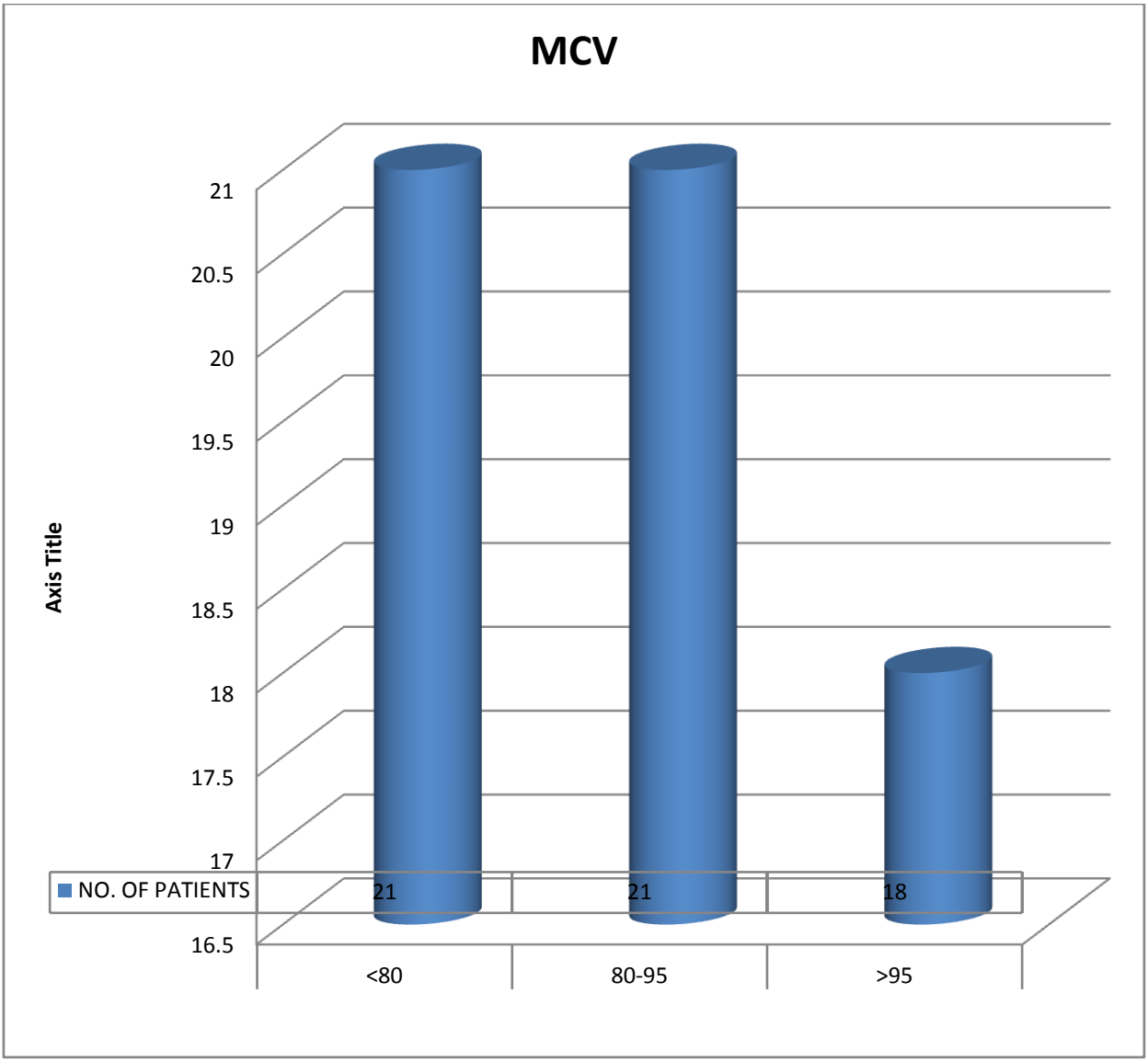
45% of people had normal differential count while 22% had neutrophilia and 33% had lymphocytosis in the study.




| Platelet Count | | |
|---|---|---|
| **COUNT** | **NO. OF PATIENTS** | **PERCENTAGE** |
| <10000 | 7 | 11.67% |
| 10000-50000 | 31 | 51.67% |
| >50000 | 22 | 36.67% |

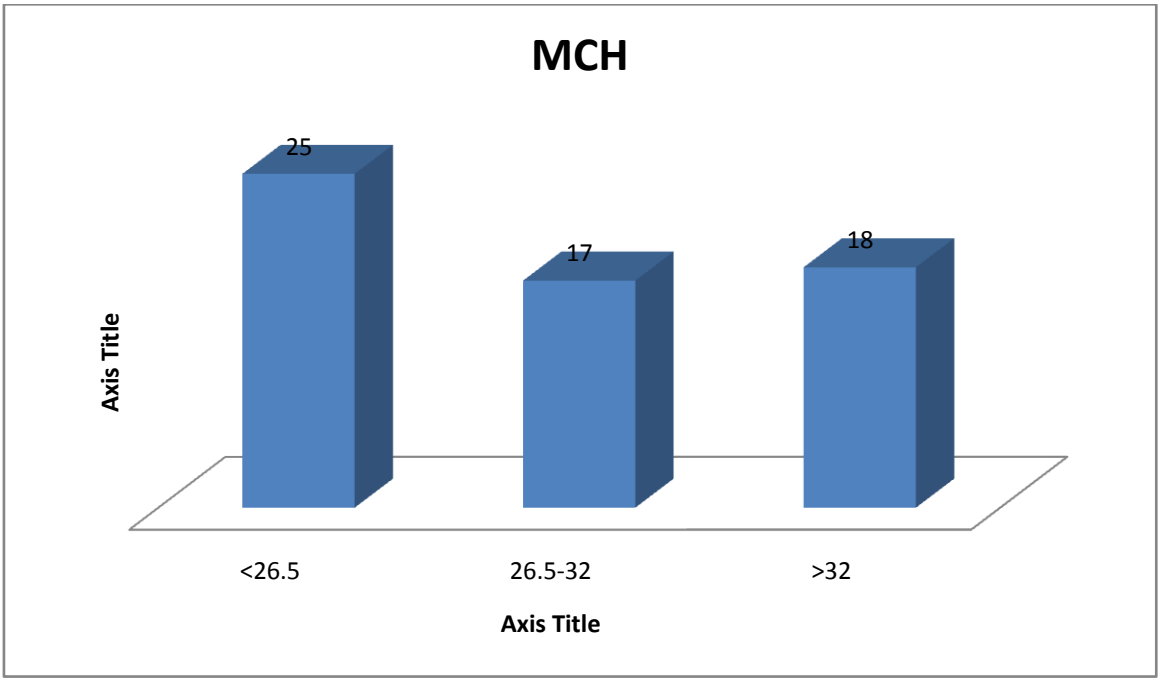
31 patients had a platelet count between 10,000- 50,000cells/mm$^3$, 22 patients had a platelet count of > 50,000cells/mm$^3$ while 7 people presented with a very low platelet count of <10,000cells/mm$^3$

Mean platelet count in the study population was found to be 40750 with a standard deviation of 24789.



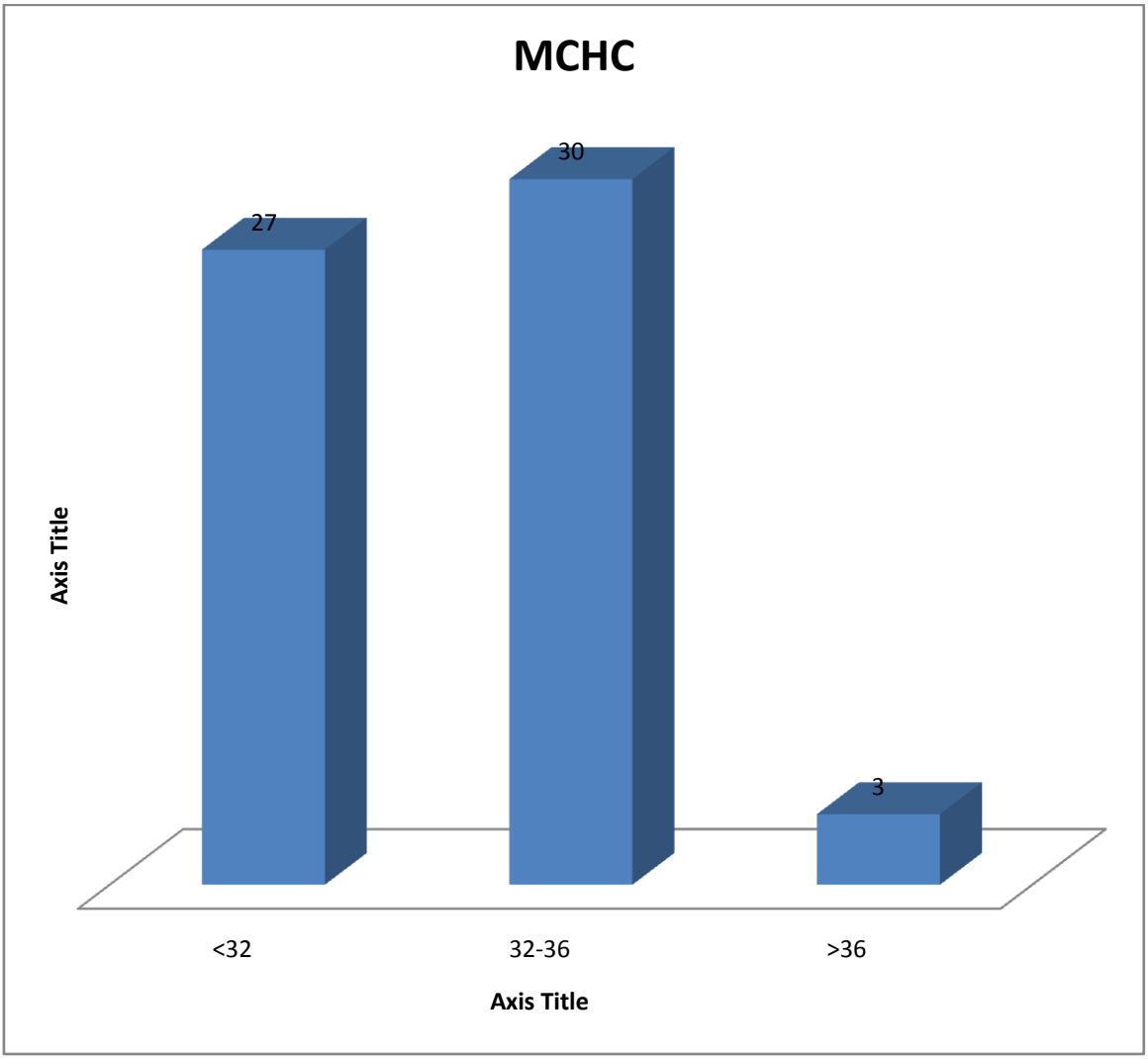

| MEAN CORPUSCULAR VOLUME | | |
|---|---|---|
| (IN FEMTO LITRES | NO. OF PATIENTS | PERCENTAGE |
| <80 | 21 | 35% |
| 80-95 | 21 | 35% |
| >95 | 18 | 30% |

30% of people presented with macrocytic anemia while 35% presented with normocytic and microcytic anemia. Average MCV was found to be 87.53+/-17.17 .



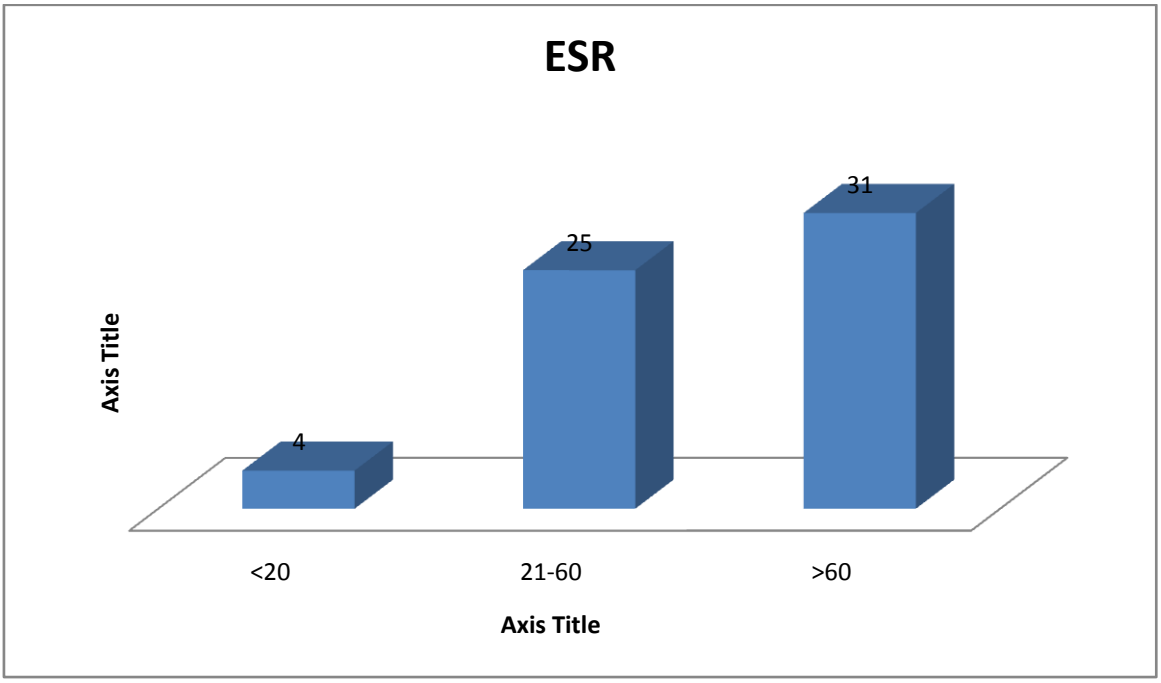

| Mean Corpuscular Haemoglobin | | |
|---|---|---|
| **In Picogram/cell** | **NO. OF PATIENTS** | **PERCENTAGE** |
| <26.5 | 25 | 41.67% |
| 26.5-32 | 17 | 28.33% |
| >32 | 18 | 30% |

Mean Corpuscular Hemoglobin was found to be 28.19pg/cell with a standard deviation of 6.68.



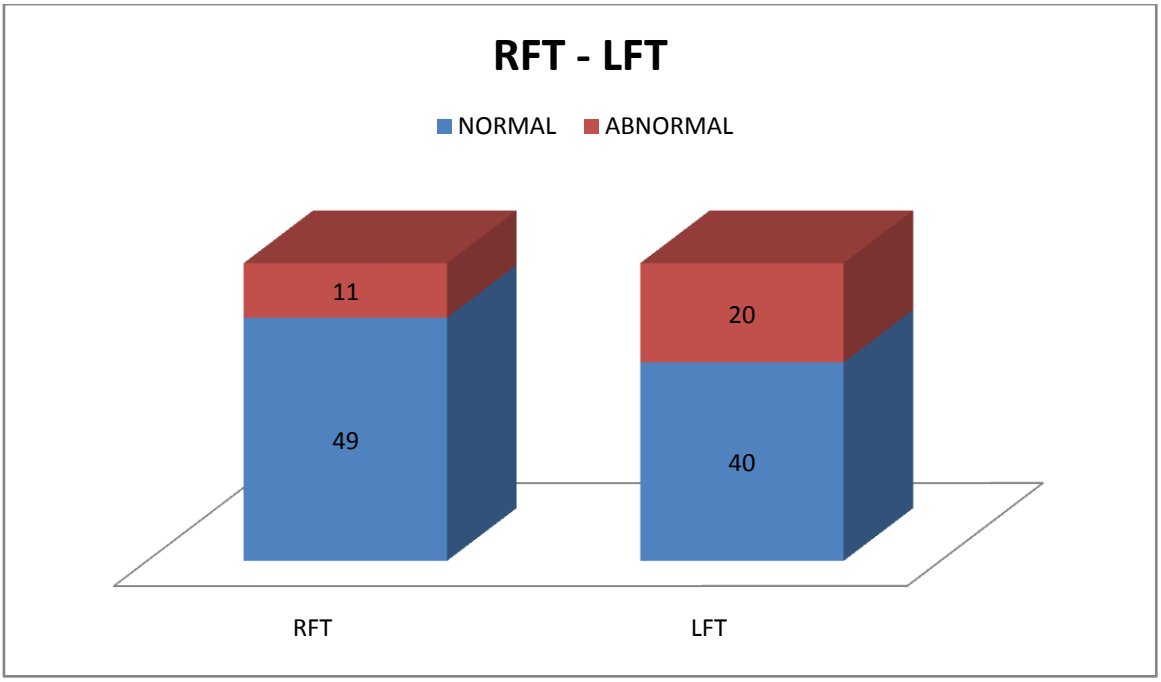

| Mean Corpuscular Hemoglobin Concentration | | |
|---|---|---|
| **In gm/dL** | **NO. OF PATIENTS** | **PERCENTAGE** |
| <32 | 27 | 45% |
| 32-36 | 30 | 50% |
| >36 | 3 | 5% |

Mean Corpuscular Hemoglobin Concentration was found to be almost equally distributed among <32gm/dL and those with 32-36gm/dL.



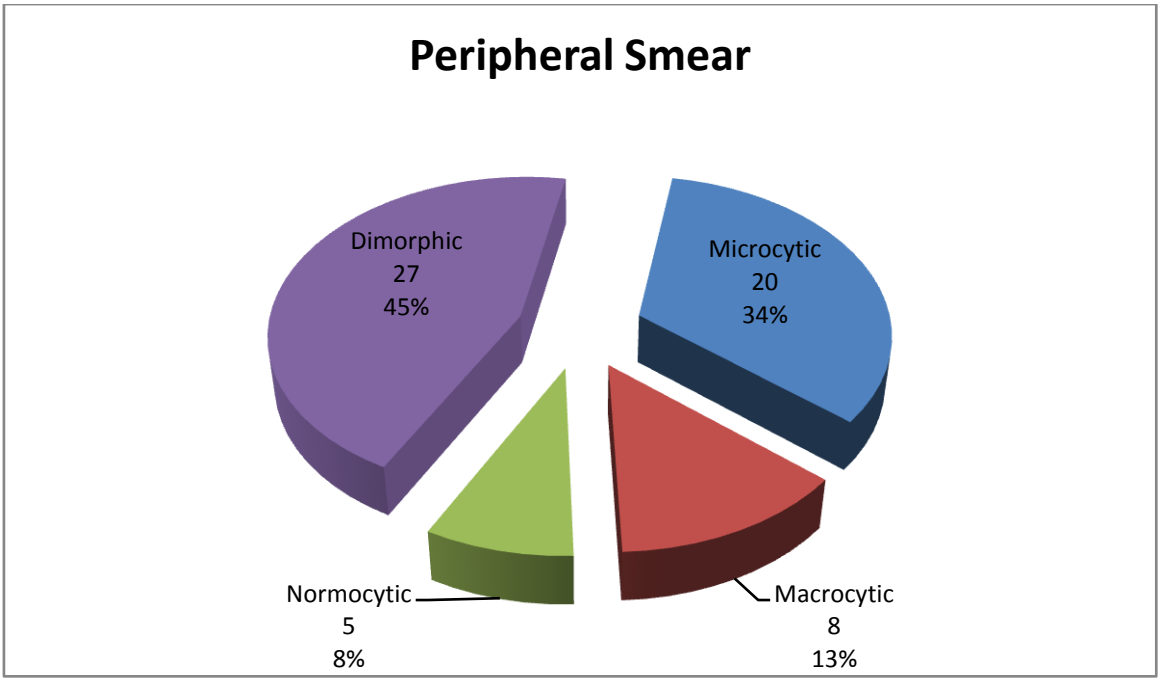

| Erythrocyte Sedimentation Rate | | |
|---|---|---|
| **MM/ FIRST HR** | **NO. OF PATIENTS** | **PERCENTAGE** |
| <20 | 4 | 6.67% |
| 21-60 | 25 | 41.67% |
| >60 | 31 | 51.67% |

Mean ESR was 65.53 with a standard deviation of 35.84.



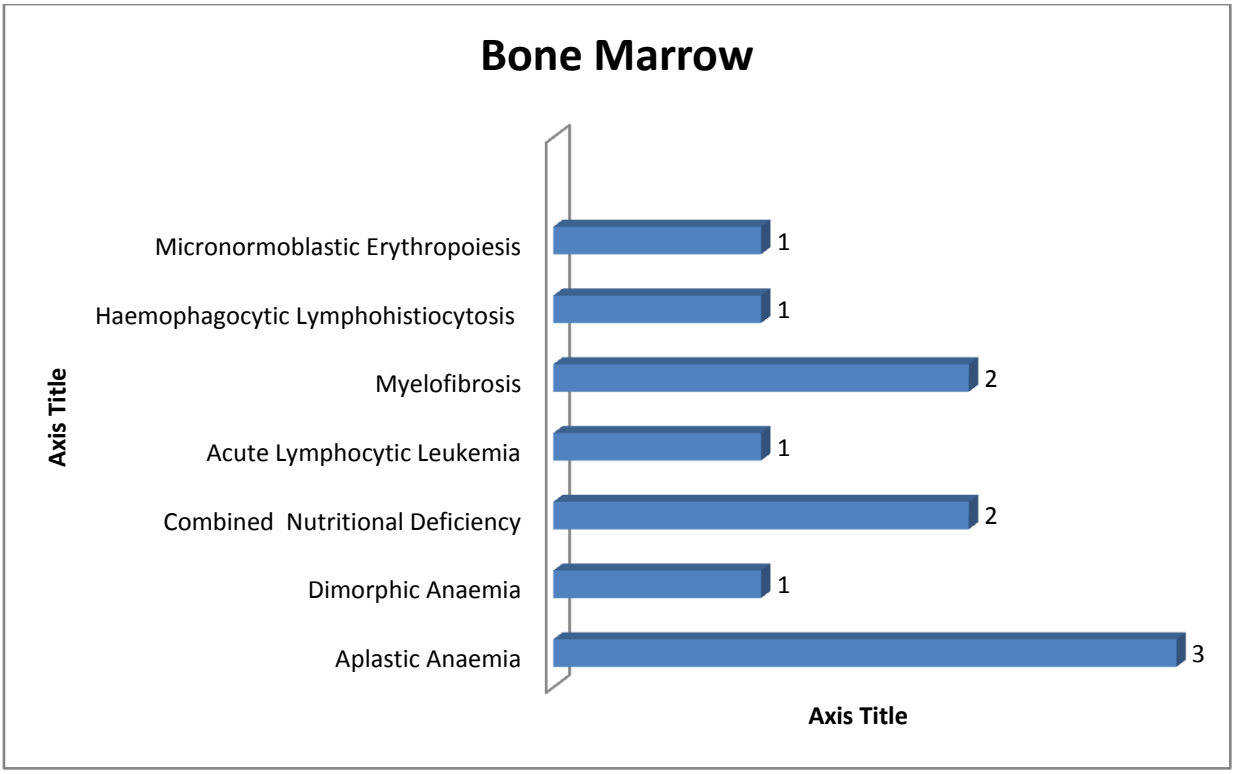

RFT was found to be normal in 49 out of 60 patients (81.5%) with 18.5% having abnormal RFT.

LFT was found to be abnormal in 33% of the study population.

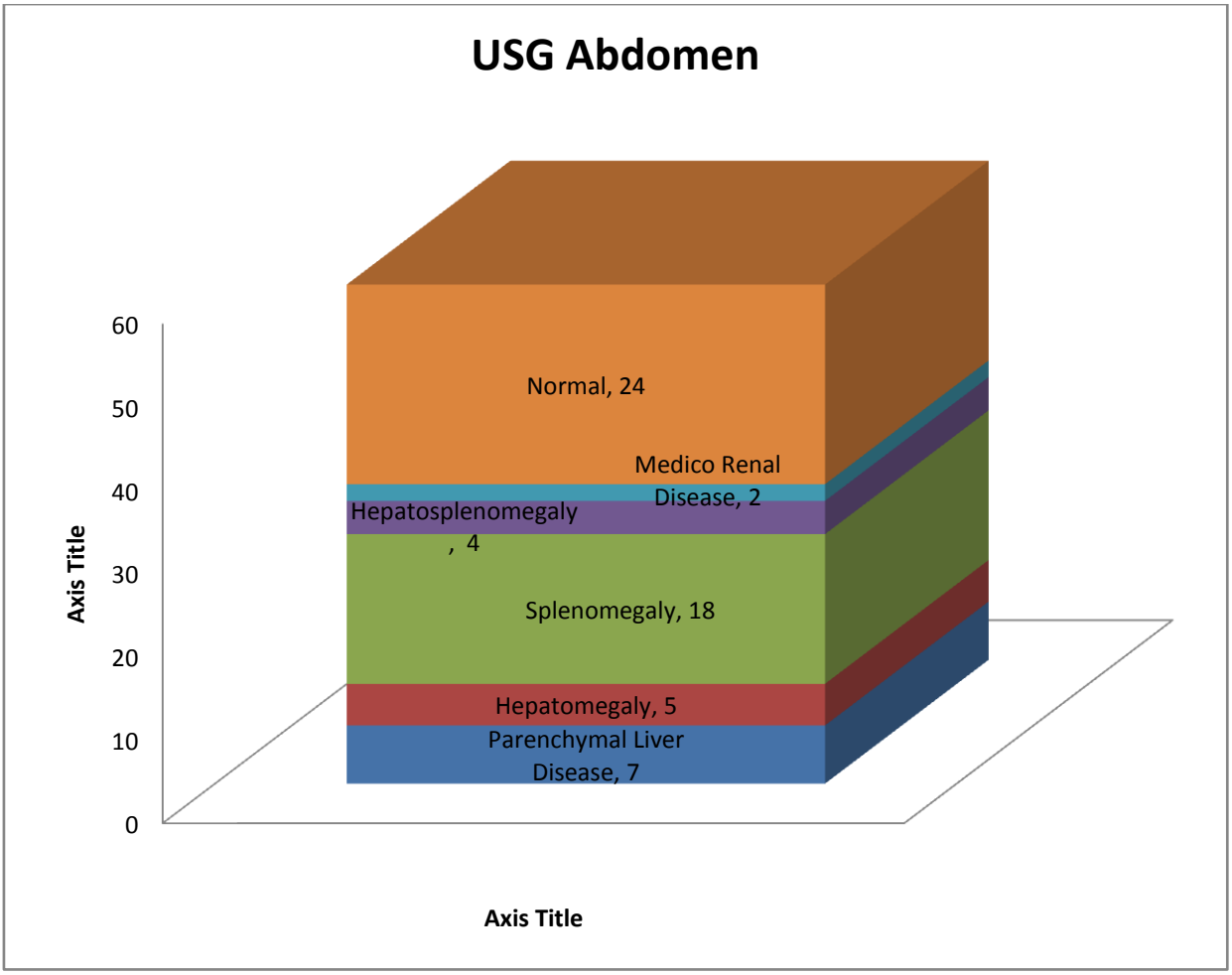



| PERIPHERAL SMEAR FINDINGS | | |
|---|---|---|
| | NO. OF PATIENTS | PERCENTAGE |
| Microcytic | 20 | 33.33% |
| Macrocytic | 8 | 13.33% |
| Normocytic | 5 | 8.33% |
| Dimorphic | 27 | 45% |

Dimorphic anemia was found to be the predominant peripheral blood picture seen in about 45% of patients. The next most common peripheral blood picture was microcytic anemia(33.33%) followed by macrocytic anemia and normocytic blood picture.

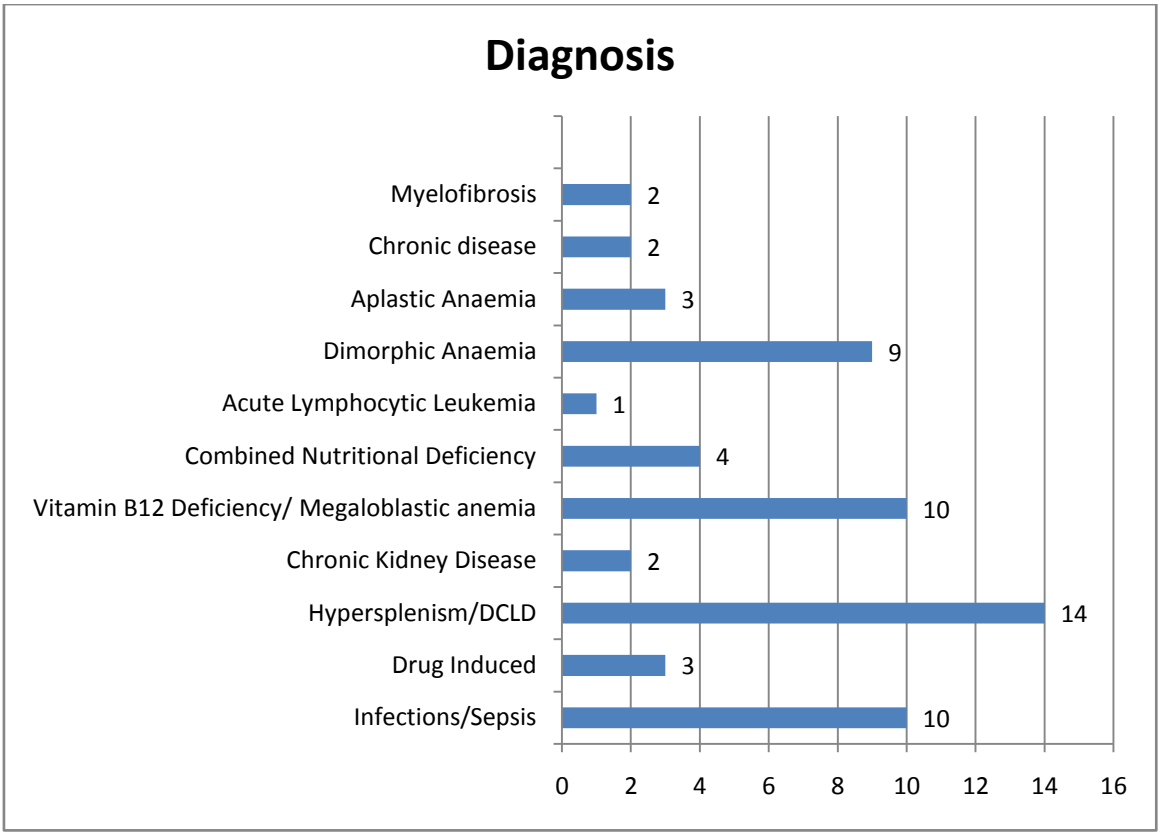


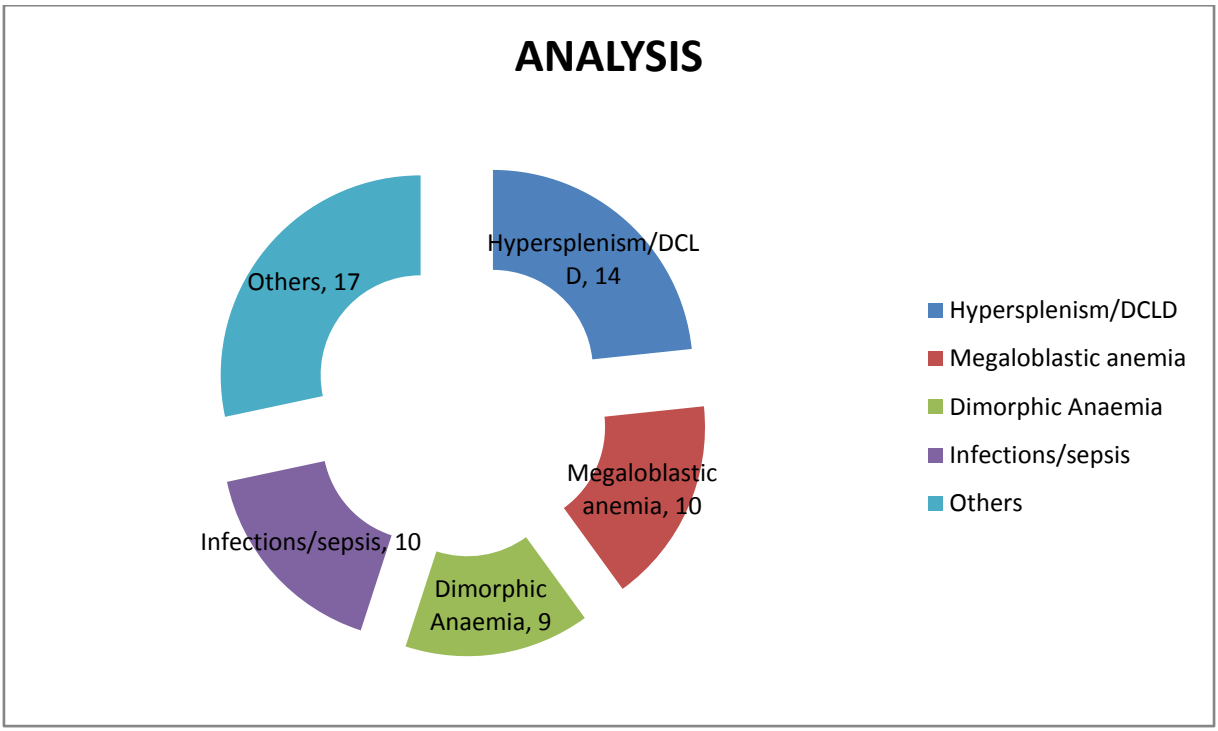

18 out of 60 patients had undergone bone marrow study. Aplastic anemia was found to be the most common peripheral blood picture followed by combined nutritional deficiency and myelofibrosis.




| Ultrasound Study of Abdomen | | |
|---|---|---|
| | **NO. OF PATIENTS** | **PERCENTAGE** |
| Splenomegaly | 18 | 30% |
| Hepatomegaly | 5 | 8.33% |
| Hepatosplenomegaly | 4 | 6.67% |
| Parenchymal Liver Disease | 7 | 11.67% |
| Medico Renal Disease | 2 | 3.33% |
| Normal | 24 | 40% |

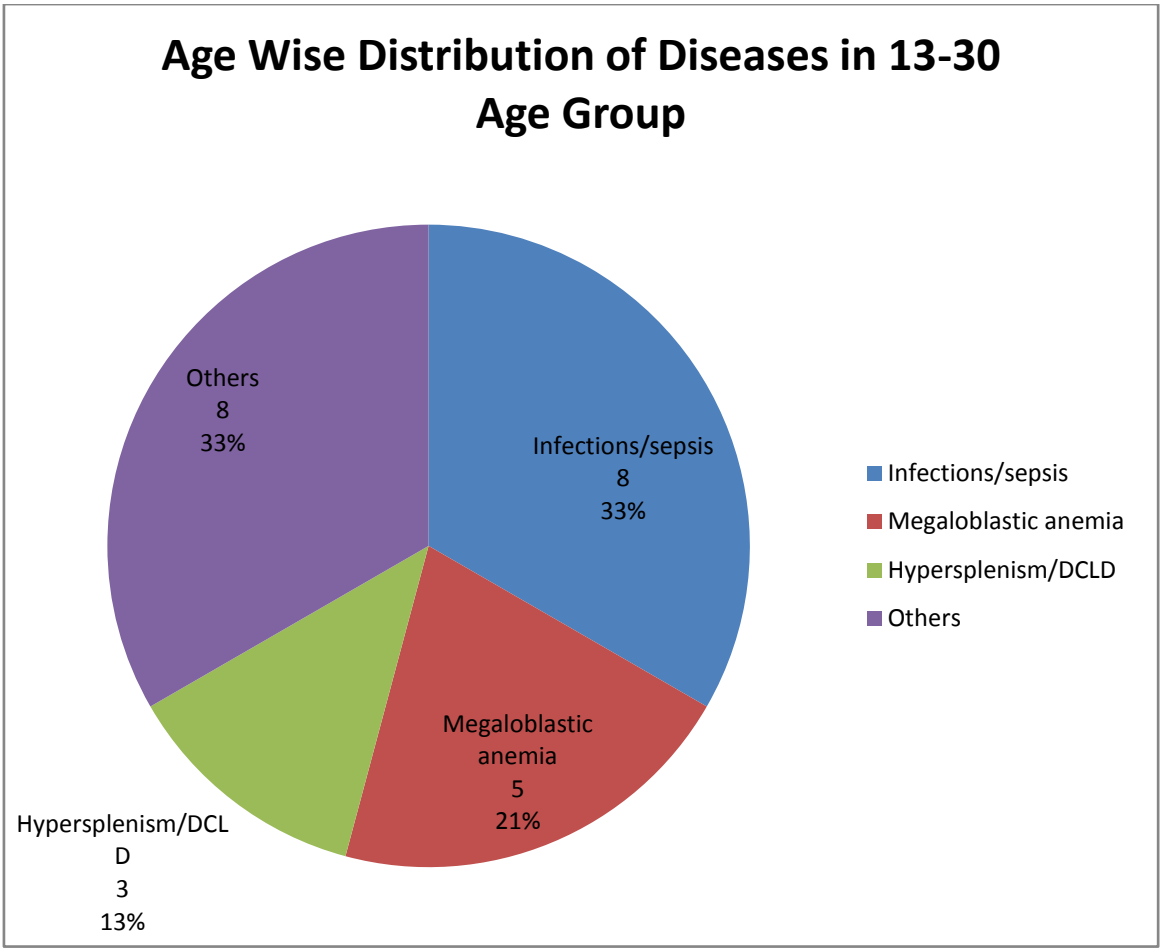
In ultrasound study of abdomen, 40% had a normal sonogram, 36.67% had enlarged spleen, 8.33% had hepatomegaly.


Diagnosis
Myelofibrosis
Chronic disease
Aplastic Anaemia
Dimorphic Anaemia
Acute Lymphocytic Leukemia
Combined Nutritional Deficiency
Vitamin B12 Deficiency/ Megaloblastic anemia
Chronic Kidney Disease
Hypersplenism/DCLD
Drug Induced
Infections/Sepsis
2
2
3
9
1
4
10
2
14
3
10
0
2
4
6
8
10
12
14
16


ANALYSIS
Others, 17
Hypersplenism/DCL D, 14
Megaloblastic anemia, 10
Dimorphic Anaemia, 9
Infections/sepsis, 10
Hypersplenism/DCLD
Megaloblastic anemia
Dimorphic Anaemia
Infections/sepsis
Others

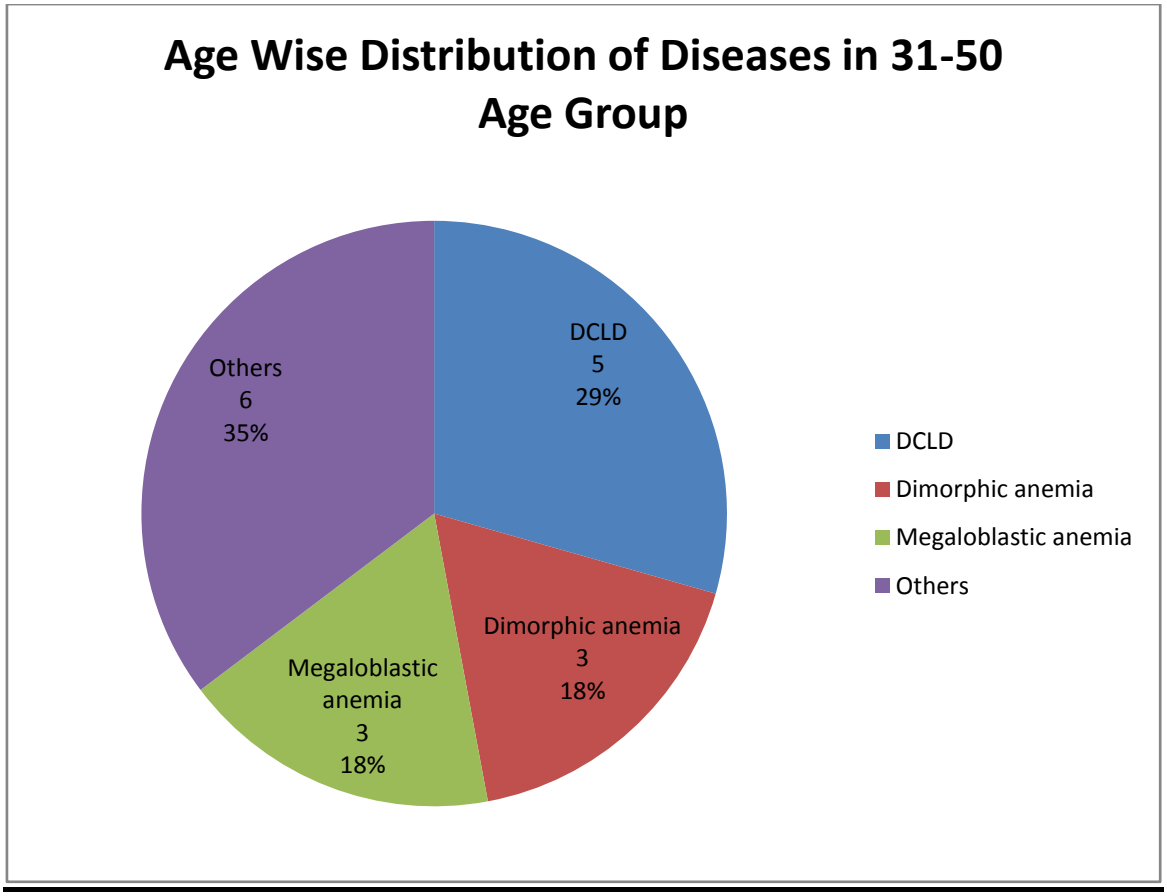
| Diagnosis | | |
|---|---|---|
| | **NO. OF PERSONS** | **PERCENTAGE** |
| Hypersplenism/DCLD | 14 | 23.33% |
| Megaloblastic Anemia | 10 | 16.67% |
| Dimorphic Anemia | 9 | 15% |
| Infections/Sepsis | 10 | 16.67% |
| Others | 17 | 28.33% |

Majority of cases of pancytopenia were found to be caused by hypersplenism with or without associated decompensated liver disease(23.33%), followed by megaloblastic anemia which accounted for 16.67% of cases. Other common causes for pancytopenia included sepsis/infections, dimorphic anemia, combined nutritional deficiencies, drug induced, aplastic anemia, myelofibrosis etc…



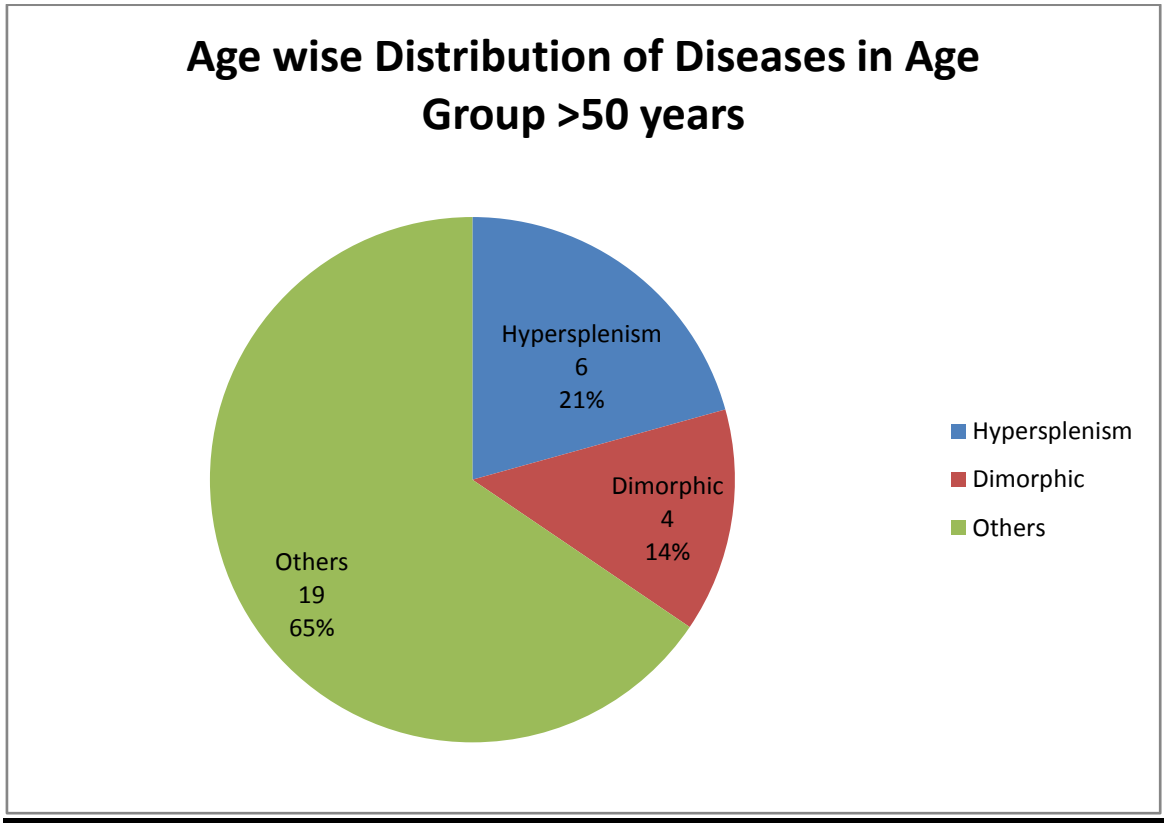

| | No Of Patients | Percentage |
|---|---|---|
| Infections/Sepsis | 8 | 33.33% |
| Megaloblastic Anemia | 5 | 20.83% |
| Hypersplenism/DCLD | 3 | 12.5% |
| Others | 8 | 33.33% |

In the age group of 13-30 years, infections/sepsis comprised maximum number of cases accounting for 33% of cases followed by megaloblastic anemia(21%).



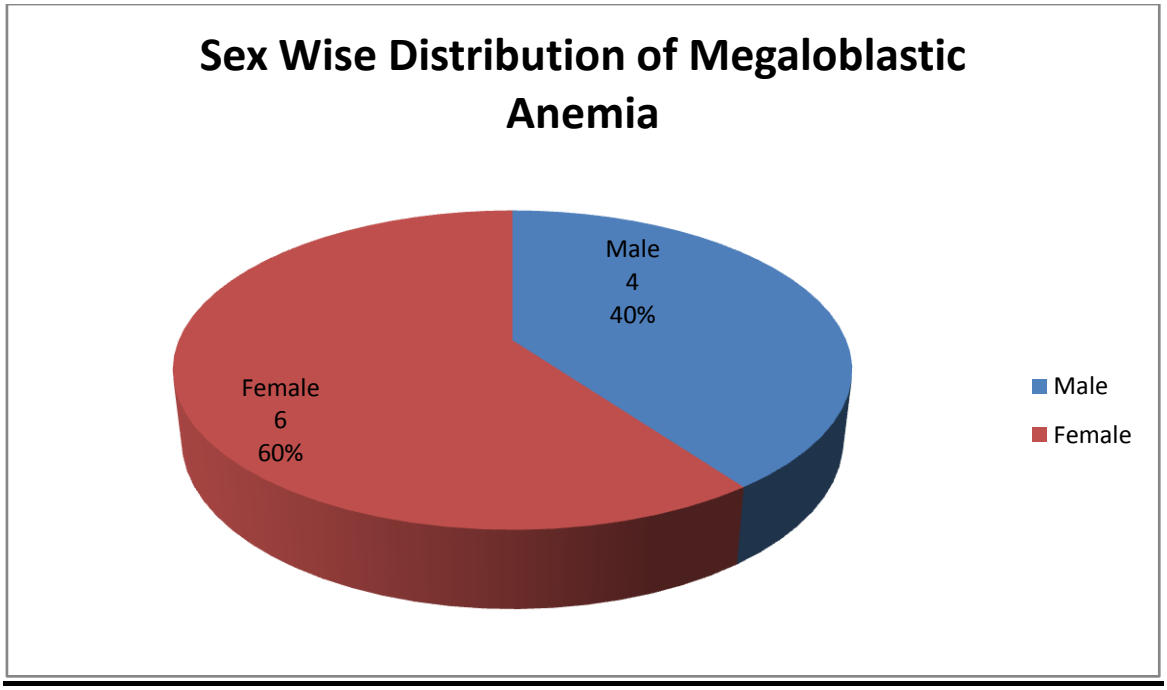

| | No of Patients | Percentage |
|---|---|---|
| Hypersplenism/DCLD | 5 | 29% |
| Dimorphic anemia | 3 | 18% |
| Megaloblastic anemia | 3 | 18% |
| Others | 6 | 36% |

In the age group of 31-50 years hypersplenism accounted for maximum number of cases with 29% followed by megaloblastic and dimorphic anemias.

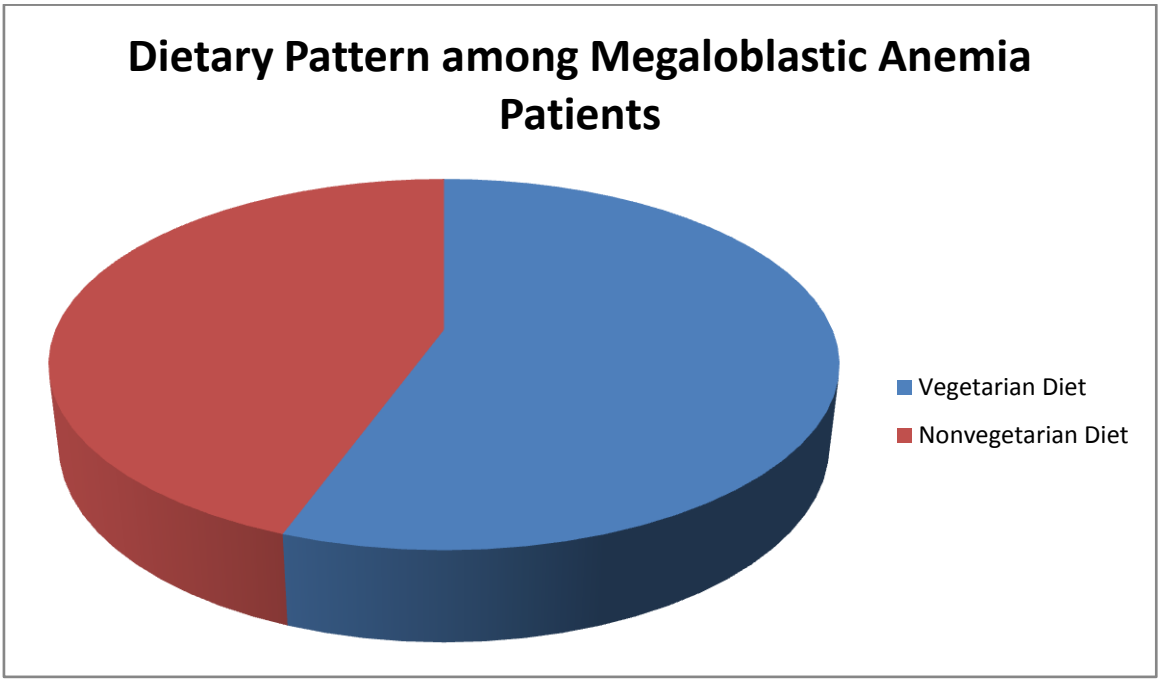



| | No of Patients | Percentage |
|---|---|---|
| Hypersplenism | 6 | 21% |
| Dimorphic anemia | 4 | 14% |
| Others | 19 | 65% |

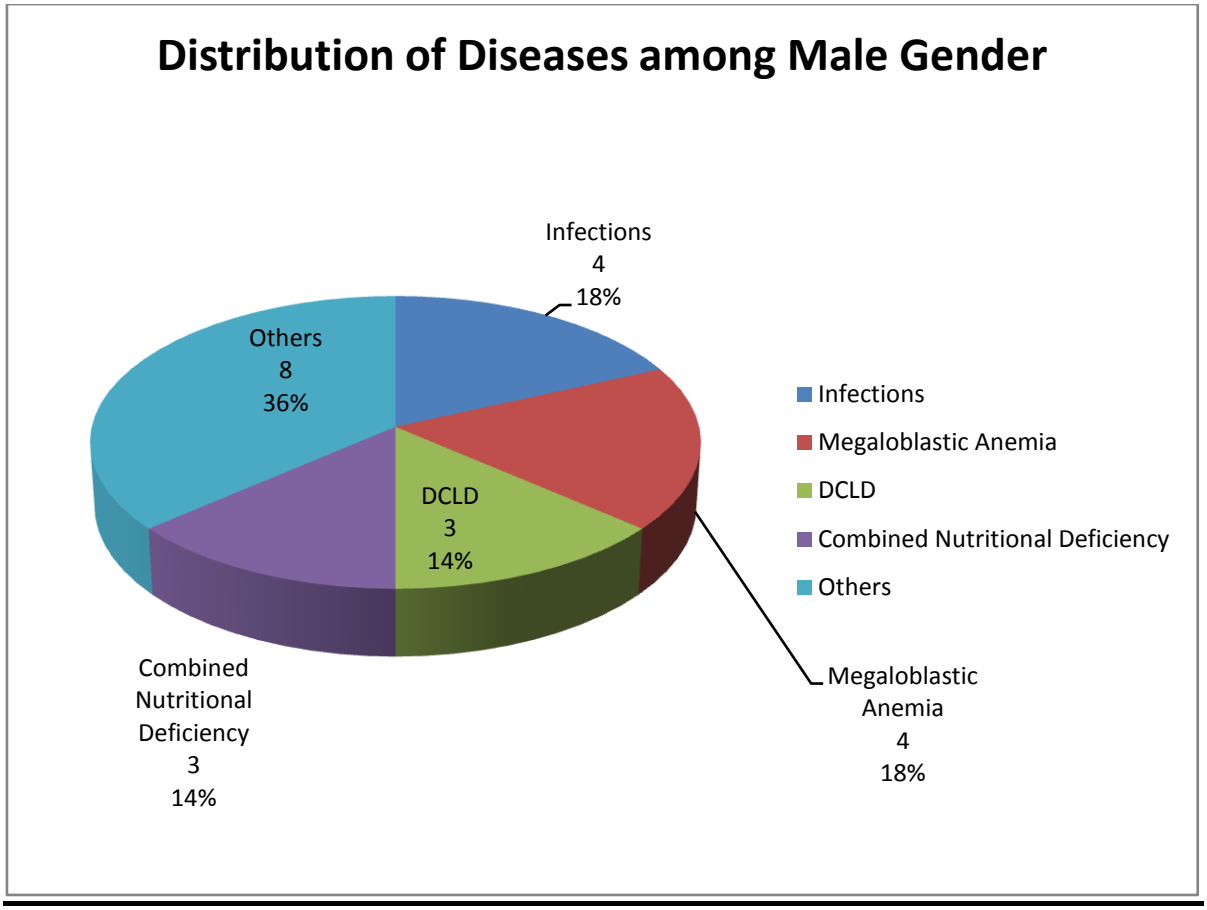
In this age group, hypersplenism accounts for maximum number of cases followed by dimorphic anemia.




Out of 10 cases of megaloblastic anemia, 6 cases(60%) were females while 4 cases(40%) comprised of males.

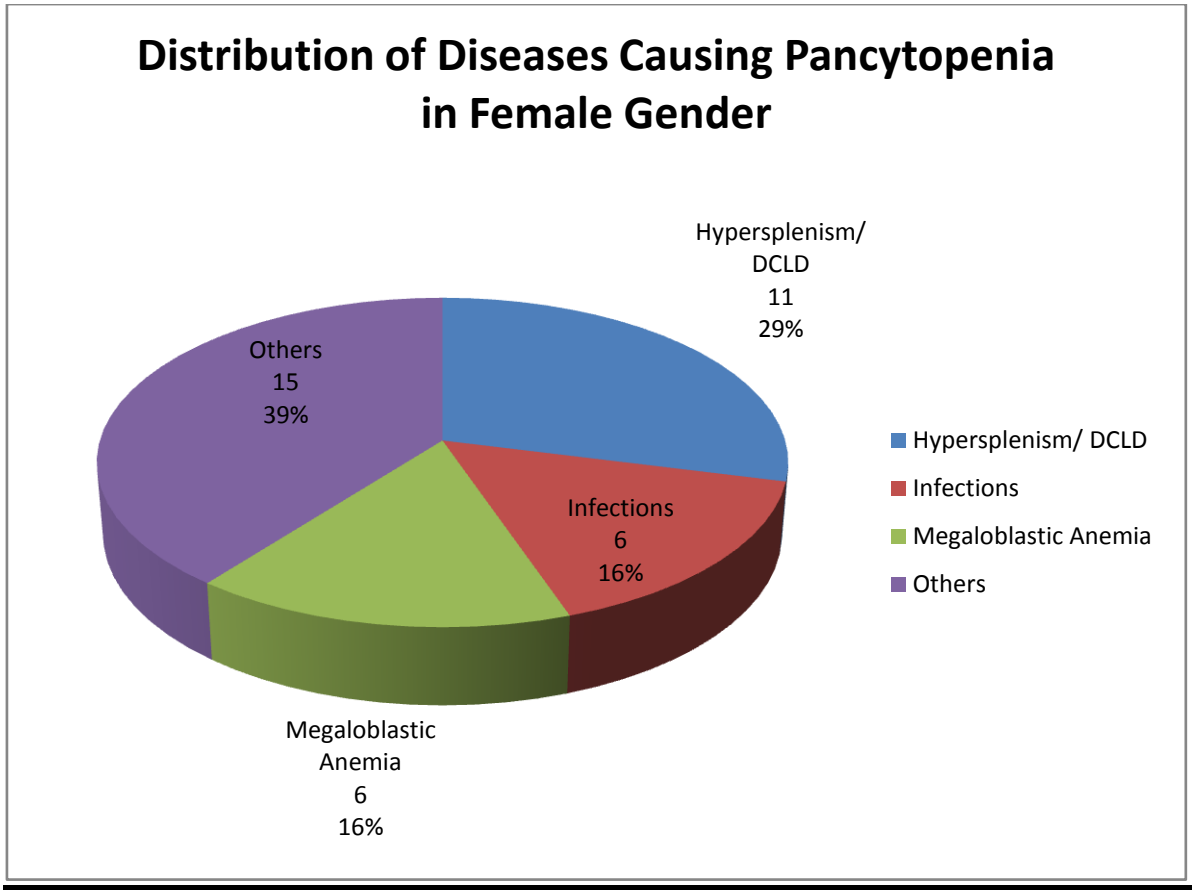



Out of 9 megaloblastic anemia cases 4 practiced a nonvegetarian diet while 5 people followed a vegetarian diet.



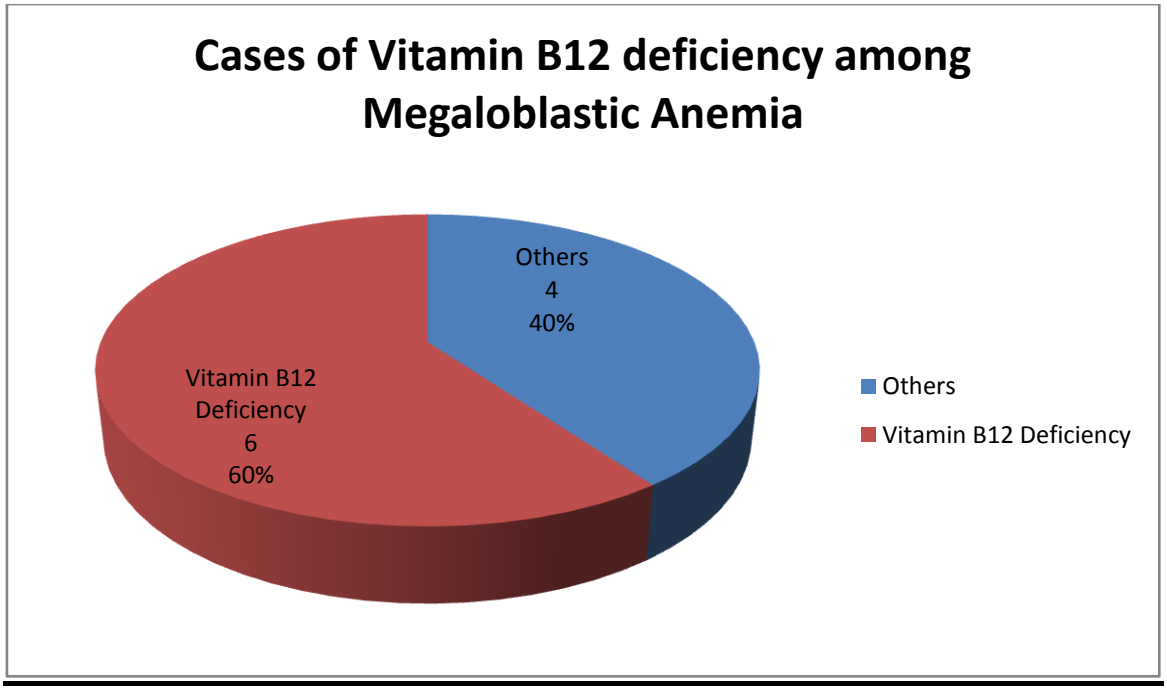

| | No of Patients | Percentage |
|---|---|---|
| Megaloblastic Anemia | 4 | 18% |
| Infections | 4 | 18% |
| Hypersplenism/DCLD | 3 | 14% |
| Combined nutritional deficiency | 3 | 14% |
| Others | 8 | 36% |

In males, megaloblastic anemia and infections comprised majority of cases followed by decompensated liver disease and combined nutritional deficiency.




| | No of Patients | Percentage |
|---|---|---|
| Hypersplenism/DCLD | 11 | 29% |
| Infections | 6 | 16% |
| Megaloblastic anemia | 6 | 16% |
| Others | 15 | 39% |

Hypersplenism accounts for majority(29%) of patients in females followed by infections(16%) and megaloblastic anemia(16%).




Out of 10 patients who had megaloblastic anemia, 6 people showed decreased levels of vitamin B12 in their blood.

# DISCUSSION & CONCLUSION

# DISCUSSION

Pancytopenia is a clinico-haematological entity encountered in our day to day practice in which all the three major formed elements of blood (RBCs, WBCs and platelets) are diminished in number. There are varying trends in its clinical pattern, treatment modalities, and outcome.

In this study around 60 cases of pancytopenia were studied. Various clinical and hematological parameters were evaluated and final diagnosis for pancytopenia was made. Clinical and haematological profile of patients with pancytopenia was studied, including their presenting symptoms and physical findings. Peripheral smear examination and ultrasound study findings were also evaluated in each case.

In the study out of 60 cases, 38 patients were females and 22 were males. Thus females formed the majority of patients, while in other studies done by Gayathri et al and Santra et al, showed a male predominance with male to female ratio of 1.2:1 and 1.47:1 respectively. Male to female ratio was 0.58:1 in this study group.

Patients were predominantly in the age group of 13-30 years (48.33%). Mean age was 38years in the study population. An Indian study published in May 2013 showed that majority (65%) of patients were in the age group of <40years. This study also showed male predominance with M:F ratio 1.6:1. Another study conducted in Iraq in 2009 showed the mean age of

pancytopenia presentation being 38yrs and had slight male predominance (M:F = 1.2:1). In another study done by Hema et al from Bengaluru also showed male predominance (60%) with most of the patients in the age group of 21 - 30 years and females aged greater than 50 were affected more. Thus this study is in compliance with most of them in the age group but sex distribution is very much different from other studies.

Percentage of patients presented with following presenting complaints namely fever, fatiguability, oedema and bleeding were 63%, 40%, 42% and 32% respectively, whereas it was asthenia (100%) and fever (28%) the predominant symptoms in the study by Nafil H[7]. In the study done by B N Gayathri et al[8] most common presentation was generalized weakness; other major complaints were breathlessness, fever and loss of weight. Pallor was present in every case. In this study 95% patients were clinically having pallor, icterus in 33%, oedema in 50%, splenomegaly in 32%, hepatomegaly in 22% and combined hepatosplenomegaly in 12%.

So the most common findings were pallor, oedema and splenomegaly. In a study by Sarode et al[5], 46% had hepatomegaly, 34% had mild splenomegaly. In comparison the study by Gayathri et al[8], the most prevalent physical finding was pallor (100%), followed by splenic enlargement (35.57%) and enlargement of liver (26.92%).

Haemoglobin values were distributed around 4-7 gm% in 45% of people, >7gm% in 27%. Mean haemoglobin was 5.74+2.17 (range- 2.3 to 9.9

gm%). While mean haemoglobin was 6.5 g/dL (range 2.9-9.2g/dL) in the study by Nafil H. Mean haemoglobin (Hb) was 5.6 +/- 1.7 g/dl in a study by Doshi D etal. In our study 73% of patients had leucocyte count in the range of 1001-3000, 23% had leucocyte count above 3000 to 4000, 4% had leucocyte count below 1000. Mean leukocyte count was 2432 with a standard deviation of 800. Lowest WBC count recorded in the study was 600 and highest 3900. In the study by Nafil H[7] , mean leucocyte count was around 2360/$mm^3$ (range 840-3360/$mm^3$) while in the study by Doshi D etal[6], mean white blood corpuscle (WBC) count was 2735 +/- 415/$mm^3$. In our study patients with platelet count in the range 10000-50000 constituted 51.67% and 50000-100000 in 36.67% with a mean platelet count of 40750 and standard deviation of 24789. Lowest platelet count was recorded as 3000 and highest being 97000. In the study by Doshi D etal[6] mean platelet count was 52,250 +/- 24,213 and in the study by Nafil H[7], mean platelet count 66 000/$mm^3$ (range 3000-123000/$mm^3$). In my study, 51.67% of patients had ESR value above 60. Similarily in the study carried out by Gayathri etal[8], ESR was elevated above 50 in around 78% of patients.

In our study, 18 patients were having MCV >95 out of which 10 had megaloblastic anaemia, out of which (6) 60% had serum B12 levels <200. So 60% of patients with megaloblastic anemia had reduced Vitamin B12 assay. In the study by Doshi D et al[6] mean MCV value was 101.2 +/- 11 in patients with megaloblastic anaemia. In a recent study, Sarode R et al[5] have analysed 139 consecutive cases of nutritional megaloblastic anaemia over a period of four and

a half years, vitamin B12 deficiency was detected in 76%, folate deficiency in 6.8%, combined B12 and folate deficiency in 8.8%; the remaining 7.8% had normal vitamin levels at presentation. Percentage of patients with megaloblastic anaemia who were having significant vitamin B12 deficiency in my study was comparable to other studies.

In our study, 45% of patients had a dimorphic blood picture, 8% patients had normocytic normochromic blood picture, 33% had microcytic hypochromic blood picture and 13% had macrocytic blood picture. In the study by Gayathri etal[7], the predominant blood picture was dimorphic anemia (37.5%), followed by macrocytic anemia (31.7%).

In our study, DCLD with associated hypersplenism(23.33%) was found to be the most common cause of pancytopenia followed by megaloblastic anemia.(16.67%). Other causes were dimorphic anemia, infections, aplastic anemia, combined nutritional deficiencies, myelofibrosis etc… In a study by Santra G[25], aplastic anaemia (20.72 %) was the most common cause of pancytopenia followed by hypersplenism associated with chronic liver disease (11.71 %). Another study by Osama et al[26], also had megaloblastic anaemia as the leading cause of pancytopenia.

In patients with aplastic anemia, hepatomegaly and splenomegaly were absent, oedema(66%) and icterus(33%) were the predominant findings. In megaloblastic anemia, oedema occured in 46%, and splenomegaly in 8% of patients. In my study, in 13-30 year age group, sepsis or infection comprised

most of cases accounting for 33% cases followed by megaloblastic anemia 21%. In 31-50 yrs age group as well as in 51-70 age group, chronic liver disease leading to hypersplenism was the most common cause of pancytopenia, followed by megaloblastic anemia.

When analyzing sex wise distribution of pancytopenia, cause of pancytopenia in males were megaloblastic anemia(18%) followed by infections and hypersplenism. In females the most common cause was found to be hypersplenism followed by infections and megaloblastic anemia. Females were having 1.5 times more prevalence of megaloblastic anemia compared to males. Totally there were 9 vegetarians, out of which 5 were having megaloblastic anaemia. Vegetarians are having more megaloblastic anemia predisposing to pancytopenia.

# CONCLUSION

In my study, it was seen that hypersplenism was the most common cause of pancytopenia. Similar to recent studies carried out by Osama et al[26] and Gayatri et al[8], megaloblastic anaemia has also emerged as a common cause of pancytopenia. Vegetarians are more predisposed to develop megaloblastic anaemia.

- Hypersplenism was the most common cause of pancytopenia in my study
- Young people contributed to the major bulk of pancytopenia cases.
- Fever, breathlessness and dependant oedema were the predominant presentations
- Pallor, oedema, splenomegaly and hepatomegaly were the predominant clinical findings
- Dimorphic blood picture was predominantly seen in peripheral blood.
- Vitamin B12 deficiency was found in about 60% of megaloblastic anemia.

## LIMITATIONS

- Only patients above 12 years of age were included in the study since Department of Medicine admits patients above 12 years of age only.
- The sample size was small; hence definite statistical analysis to find out different causal factors was not feasible.
- The period of study was only 1 year. Long term follow up study is also required to correctly establish the etiology.
- Transient pancytopenia can occur following various infections.
- Many patients are missed because only inpatients were included in the study.

# SUGGESTIONS

- A detailed follow up study to analyze the etiologies for pancytopenia for sufficiently long duration for better analysis and hypothesis.
- A comparative study using healthy controls could be better to establish the relation of dietary deficiency with the etiologies other than nutritional anemia.
- The issue why megaloblastic anemia is more common among females is to be studied in detail to bring out any social issues including gender discrimination.
- Since megaloblastic anaemia with vitamin B12 deficiency is common, dietary habits should be modified.
- Since pregnancy is an important cause for pancytopenia, a study involving them as study group with special emphasis on the precipitating factors should also be done.

## ABBREVIATIONS

PMF=Primary Myelofibrosis

DCLD= Decompensated Chronic Liver Disease

CKD=Chronic Kidney Disease

MDS=Myelodysplastic Syndrome

RBC= Red Blood Corpuscle

WBC=White Blood Corpuscle

SLE=Systemic Lupus Erythematosis

TB= Tuberculosis

Fl=Femtolitres

Pg/ml=Pictogram/ml

MCV=Mean Corpuscular Volume

MCH=Mean Corpuscular Haemoglobin

MCHC=Mean Corpuscular Hemoglobin Concentration

HTN = Hypertension

PCV=Packed Cell Volume

ESR=Erythrocyte Sedimentation Rate

RFT=Renal Function Test

LFT= Liver Function Test

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# ANNEXURES

**ANNEXURE 1**

**PROFORMA**

SL no: Contact no:

Name: IP No:

Age: Unit:

Sex: Date of Admission:

Occupation: Date of Discharge :

**History**

| | |
|---|---|
| Fever | |
| Spontaneous mucosal bleeding | |
| Petechiae, purpura | |
| Fatigability | |
| Shortness of breath | |
| Chestpain | |
| Infections | |
| Lymphadenopathy | |
| Cough | |
| Dependent oedema | |
| Abdominal pain | |
| Weight loss | |
| Onset | |
| Drug intake | |

**Past history**

DM/HTN/TB/LIVER DISEASE/CANCER

**Family history** : TB/LIVER DISEASE/CANCER

**Personal History**: Smoker alchoholic Veg/non veg

Appetite High risk behavior

**General Examination**

- Pallor :yes/no
- Icterus :yes/no
- Cyanosis :yes/no
- Clubbing :yes/no
- Lymphadenopathy :yes/no
- Edema :yes/no

**Vitals**

- Blood pressure :
- Pulse rate :
- Respiratory rate :

**Examination**

**Eye examination** Retinal haemorrhage

**Oral examination**

Petechiae : Gingival hyperplasia :

Stomatitis/cheilitis: Oral candidiasis :

**Respiratory Examination**

Clubbing

**Abdominal examination** Lymphadenopathy/ Hepatomegaly/ Splenomegaly

**Skin examination**

Malar rash

Purpura /bruising

Hyperpigmentation, café au lait , Skin nodules

**Musculoskeletal examination**

Short Stature : Abnormal thumbs:

**INVESTIGATIONS**

Hemoglobin: Red Blood Cell Count:

Total Leukocyte Count: Differential Leukocyte Count:

Platelet Count:

Mean Corpuscular Volume (MCV) :

Mean Corpuscular Haemoglobin (MCH):

Mean Corpuscular Hemoglobin Concentration (MCHC):

Packed Cell Volume (PCV):

Erythrocyte Sedimentation Rate (ESR):

Peripheral Smear:

Bone Marrow Aspiration If Needed:

Chest X Ray:

USG Abdomen:

Renal Function Test:

Liver Function Test:

| SL NO | NAME | AGE | SEX | IP No | PRESENTING COMPLAINTS | | | | | | | | | PAST HISTORY | | | | | | | PERSONAL HISTORY | | | DIET HISTORY |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Fever | Mucosal Bleeding | Fatigu-ability | Breath-lessness | Cough | Dependent Oedema | Abdominal Pain | Petechiae /Purpura | Chest Pain | Diabetes | CKD | Hyper-tension | TB | CAHD | LIVER DISEASE | None | Smoking | Alcohol | None | |
| 1 | Arumugakani | 40 | F | 6399 | Y | | | Y | Y | | | | | | | | | | | Y | | | Y | Non-Vegetarian |
| 2 | Kalaiselvi | 26 | F | 7735 | Y | | | Y | | Y | | | | | | | | | | Y | | | Y | Non-Vegetarian |
| 3 | Ranganathan | 68 | M | 7960 | Y | | | Y | Y | | | | | Y | | | Y | | | | Y | | | Non-Vegetarian |
| 4 | Annamalaiyamma | 20 | F | 8908 | Y | | Y | | | | Y | | | | | | | | | Y | | | Y | Non-Vegetarian |
| 5 | Murikeshveri | 22 | F | 8996 | Y | | Y | Y | | | | | | | | | | | | Y | | | Y | Vegetarian |
| 6 | Sudalaimuthu | 68 | M | 9571 | | | | Y | | Y | | | | | Y | | | | | | Y | | | Non-Vegetarian |
| 7 | Balasundari | 18 | F | 10147 | Y | Y | | | | | Y | Y | | | | | | | | Y | | | Y | Non-Vegetarian |
| 8 | Mariammal | 33 | F | 10333 | | | | Y | Y | Y | Y | | | | | | | | | Y | | | Y | Non-Vegetarian |
| 9 | Pushpa | 30 | F | 11385 | Y | Y | Y | | | | | Y | | | | | | | | Y | | | Y | Non-Vegetarian |
| 10 | Saraswathi | 56 | F | 42276 | Y | | | | | | | | | | | | | | | Y | | | Y | Non-Vegetarian |
| 11 | Palaniammal | 21 | F | 12543 | Y | | Y | Y | | Y | Y | | | | | | | | | Y | | | Y | Non-Vegetarian |
| 12 | Marisamy | 19 | M | 14400 | Y | | | | Y | | | | | | | | | | | Y | | | Y | Non-Vegetarian |
| 13 | Sally | 19 | M | 14659 | Y | | | | Y | | | | | | | | | | | Y | | | Y | Non-Vegetarian |
| 14 | Arumugathai | 45 | F | 15128 | Y | Y | | | Y | | Y | | | | | | | | | Y | | | Y | Non-Vegetarian |
| 15 | Esakkiammal | 25 | F | 15365 | Y | | | | | | | | | | | | | | | Y | | | Y | Non-Vegetarian |
| 16 | Jaya Ganesh | 17 | M | 12583 | Y | | | | Y | | Y | | | | | | | | | Y | | | Y | Non-Vegetarian |
| 17 | Samidurai | 40 | M | 45729 | Y | Y | | | | | | | | | | | | | | Y | | Y | | Non-Vegetarian |
| 18 | Subharangitha | 20 | F | 46267 | Y | | | | | | Y | | | | | | | | | Y | | | Y | Non-Vegetarian |
| 19 | Vijayalakshmi | 47 | F | 48284 | | | Y | | | Y | Y | | | | | | | | Y | | | | Y | Non-Vegetarian |
| 20 | Parvati | 70 | F | 47507 | | | | Y | | Y | | | | | | | | | | Y | | | Y | Vegetarian |
| 21 | Shekhar | 38 | M | 24122 | | Y | Y | Y | | | | | | | | | | | | Y | | | Y | Non-Vegetarian |
| 22 | Arumugakani | 22 | F | 26983 | Y | | Y | Y | | Y | | | Y | | | | | | | Y | | | Y | Non-Vegetarian |
| 23 | Chellammal | 75 | F | 26313 | | | | Y | | | Y | | | | | | | | | Y | | | Y | Vegetarian |
| 24 | Mariammal | 42 | F | 26711 | Y | | Y | Y | Y | | | | | | | | | | | Y | | | Y | Non-Vegetarian |
| 25 | Chellammal | 30 | F | 26752 | Y | Y | Y | Y | | | | | | | | | | | | Y | | | Y | Non-Vegetarian |
| 26 | Shanmugam | 86 | M | 26861 | Y | Y | Y | Y | | | | | Y | | | Y | | Y | | | Y | Y | | Non-Vegetarian |
| 27 | Sita Lakshmi | 29 | F | 26964 | | | | | | | Y | | | | | | Y | | | | | | Y | Non-Vegetarian |
| 28 | Vasuki | 27 | F | 26773 | Y | Y | | | | | | | | | | | | | | Y | | | Y | Non-Vegetarian |
| 29 | Subbuthai | 47 | F | 27312 | | | | | | Y | Y | | | | | | | | Y | | | | Y | Non-Vegetarian |
| 30 | Mallika | 50 | F | 27565 | Y | Y | Y | | | | | | | | | | | | | Y | | | Y | Non-Vegetarian |
| 31 | Thilakavathy | 17 | F | 27962 | Y | | | | | | Y | | | | | | | | | Y | | | Y | Non-Vegetarian |
| 32 | Priyanka | 17 | F | 30352 | | | Y | | | | | | | | | | | | | Y | | | Y | Vegetarian |
| 33 | Indira | 17 | F | 28574 | Y | Y | | Y | | Y | | | Y | | | | | | | Y | | | Y | Vegetarian |
| 34 | Mariya Yovan | 18 | M | 28234 | Y | | | | Y | | Y | | | | | | | | Y | | | Y | | Non-Vegetarian |
| 35 | Mariya Jose | 32 | M | 43255 | Y | | | | | | | | | | Y | Y | | | | | | | Y | Non-Vegetarian |
| 36 | Karuppusamy | 33 | M | 30414 | Y | | | | | | | | | | | | | | | Y | | | Y | Non-Vegetarian |
| 37 | Vasantha | 59 | F | 43065 | Y | | | Y | | Y | | | | | | | | | | Y | | | Y | Vegetarian |
| 38 | Hameeda Banu | 28 | F | 30689 | | Y | Y | | | | | | | | | | | | | Y | | | Y | Non-Vegetarian |
| 39 | Krishnaveni | 23 | F | 31542 | Y | Y | | Y | | | | | | | Y | | | | | | | | Y | Non-Vegetarian |
| 40 | Selvi | 30 | F | 34790 | Y | Y | | Y | | | | | | | | | | | | Y | | | Y | Non-Vegetarian |
| 41 | Parvati | 44 | F | 31673 | | | Y | Y | | Y | Y | | | | | | | | Y | | | | Y | Non-Vegetarian |
| 42 | Mariyatholan | 55 | M | 35145 | | Y | Y | | | | Y | | | Y | | | | | | | | | Y | Non-Vegetarian |
| 43 | Anthony | 64 | M | 35986 | Y | | | | | Y | Y | | | Y | | | | | | | Y | Y | | Non-Vegetarian |
| 44 | Thirumeni | 24 | M | 42675 | Y | Y | Y | Y | | | | | | | | | | | | Y | Y | | | Vegetarian |
| 45 | Nilavati | 70 | F | 44721 | | | Y | Y | | Y | | | | | | Y | | | | | | | Y | Non-Vegetarian |
| 46 | Tamilselven | 30 | M | 44844 | Y | Y | Y | | | | | | | | | | | | | Y | Y | | | Non-Vegetarian |
| 47 | Subramanian | 52 | M | 36152 | Y | Y | | Y | | Y | | | | | | | | | | Y | Y | | | Vegetarian |
| 48 | Ramasubbu | 30 | M | 36760 | Y | | | | | | | | | | | | | | | Y | | | Y | Non-Vegetarian |
| 49 | Parajyothy | 50 | F | 44671 | | | Y | Y | | Y | | | | | | | | | | Y | Y | | | Non-Vegetarian |
| 50 | Subramani | 58 | M | 33715 | | | | Y | | Y | | | | | | | | | | Y | Y | | | Non-Vegetarian |
| 51 | Malathi | 32 | F | 38305 | Y | | | | | Y | | | | | | | | | | Y | | | Y | Non-Vegetarian |
| 52 | Leelavati | 68 | F | 38386 | | | Y | Y | | Y | | | Y | | | Y | | Y | | | | | Y | Non-Vegetarian |
| 53 | Suresh Kumar | 13 | M | 39076 | Y | | Y | Y | | Y | Y | | | | | | | | | Y | | | Y | Non-Vegetarian |
| 54 | Sivaramakrishnan | 14 | M | 39497 | Y | Y | | | Y | | | | | | | | | | | Y | | | Y | Non-Vegetarian |
| 55 | Muppidathy | 45 | F | 53627 | Y | | | | Y | Y | Y | | Y | | | | | | | Y | | | Y | Non-Vegetarian |
| 56 | Kanakammal | 25 | F | 41979 | Y | | | Y | | | Y | | | | | | | | | Y | | | Y | Vegetarian |
| 57 | Gandhimati | 28 | F | 39996 | Y | | Y | Y | Y | Y | | | Y | | | | | | | Y | | | Y | Non-Vegetarian |
| 58 | Moothammal | 61 | F | 54053 | | Y | Y | Y | | Y | | | | | | | | | Y | | | Y | | Non-Vegetarian |
| 59 | Murugan | 48 | M | 54498 | | | | | | Y | | | | | | | | | | Y | Y | Y | | Non-Vegetarian |
| 60 | Muhammed Sahib | 48 | M | 54118 | | Y | | | | | Y | | | | | | | | | Y | | | Y | Non-Vegetarian |

| GENERAL EXAMINATION | | | | SYSTEMIC EXAMINATION | | | LAB | | | | | | | | | | | PATHOLOGY | | USG ABDOMEN | DIAGNOSIS |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Pallor | Icterus | Lymphad eno-pathy | Oedema | Hepato-megaly | Spleno-megaly | Both | Hemoglob in | RBC Count | Total Count | Differenti al Count | Platelet | MCV | MCH | MCHC | PCV | ESR | RFT | LFT | Peripheral Smear | Bone Marrow | | |
| | | | | | Y | | 9.7 | 4.38 | 2200 | Normal | 60000 | 87 | 26 | 30 | 38 | 80 | Normal | Normal | Dimorphic | | Splenomegaly | Infection |
| Y | | | Y | | | | 3.9 | 1.28 | 3200 | Normal | 33000 | 90 | 29.4 | 32.7 | 11.7 | 150 | Normal | Normal | Dimorphic | | Normal | Chronic Kidney Disease |
| Y | Y | Y | | | | | 3.1 | 0.9 | 2300 | ymphocytos | 27000 | 102 | 34 | 33 | 9.2 | 67 | Abnormal | Abnormal | Macrocytic | | Normal | Drug Induced |
| Y | Y | | | | | | 6.9 | 1.82 | 2200 | Normal | 23000 | 122.8 | 42.6 | 34.7 | 19.3 | 26 | Normal | Abnormal | Macrocytic | | Splenomegaly | Megaloblastic Anemia |
| Y | | | | | | | 3.6 | 1.73 | 2200 | Neutrophili | 35000 | 67 | 26 | 30 | 62.3 | 150 | Normal | Normal | Microcytic | | Splenomegaly | Hypersplenism/DCLD |
| Y | | | Y | | | | 2.4 | 0.7 | 1600 | ymphocytos | 6000 | 68 | 24 | 30 | 7.3 | 73 | Abnormal | Normal | Microcytic | | Medico Renal Disease | Chronic Kidney Disease |
| Y | | | | | | | 4.4 | 2.19 | 3300 | Normal | 7000 | 76.2 | 21.8 | 28.6 | 17.3 | 64 | Normal | Normal | Microcytic | | Normal | Infection |
| Y | | | Y | | Y | | 4.5 | 2.17 | 3700 | Normal | 56000 | 76.4 | 29.4 | 30.8 | 16.9 | 100 | Normal | Normal | Dimorphic | | Splenomegaly | Hypersplenism/DCLD |
| Y | | | | | | Y | 5 | 1.54 | 3500 | ymphocytos | 33000 | 102 | 33.1 | 32.5 | 15.3 | 74 | Normal | Normal | Dimorphic | | Splenomegaly | Hypersplenism/DCLD |
| Y | | | | | | | 7 | 2.42 | 1000 | Neutrophili | 50000 | 87.7 | 25.8 | 32.9 | 21.3 | 94 | Normal | Normal | Normocytic | | Parenchymal Liver Disease | Combined Nutritional Deficiency |
| Y | Y | | | | | Y | 3 | 0.86 | 2100 | Normal | 78000 | 115.1 | 34.9 | 30.3 | 9.9 | 145 | Normal | Abnormal | Macrocytic | | Splenomegaly | Hypersplenism/DCLD |
| Y | | | | | | | 6 | 1.7 | 3900 | ymphocytos | 19000 | 104 | 34.7 | 33.3 | 18 | 50 | Normal | Abnormal | Dimorphic | Dimorphic Anaemia | Normal | Dimorphic Anaemia |
| Y | | | | | | | 8.1 | 2.5 | 2600 | Neutrophili | 53000 | 98.4 | 32.4 | 32.9 | 24.6 | 50 | Normal | Abnormal | Dimorphic | | Splenomegaly | Infection |
| Y | | | | | | | 6.5 | 2.05 | 2200 | Normal | 61000 | 95.6 | 31.7 | 33.2 | 19.6 | 48 | Normal | Normal | Dimorphic | | Normal | Dimorphic Anaemia |
| Y | | | Y | | | | 8.3 | 2.5 | 2000 | Normal | 60000 | 95.3 | 32.7 | 34.3 | 24.2 | 42 | Normal | Normal | Dimorphic | | Normal | Dimorphic Anaemia |
| Y | | | | | | | 9.2 | 4.53 | 2500 | ymphocytos | 71000 | 84 | 28 | 32.4 | 32.7 | 28 | Normal | Normal | Normocytic | | Normal | Chronic Disease |
| Y | | | | | | | 8.1 | 3 | 2500 | Normal | 37000 | 86 | 27 | 31 | 25.8 | 32 | Normal | Normal | Microcytic | Combined Nutritional Deficiency | Splenomegaly | Combined Nutritional Deficiency |
| Y | | | Y | | | | 3.4 | 1.76 | 1200 | ymphocytos | 27000 | 72 | 22 | 28 | 10.5 | 82 | Normal | Normal | Microcytic | Aplastic Anaemia | Normal | Aplastic Anaemia |
| Y | Y | | Y | | | Y | 4.4 | 2.77 | 1300 | Normal | 14000 | 60 | 15 | 26 | 16.7 | 73 | Normal | Abnormal | Microcytic | | Parenchymal Liver Disease | Hypersplenism/DCLD |
| Y | Y | | | | | | 5.6 | 2.79 | 2700 | Normal | 64000 | 72 | 20 | 27 | 20.1 | 64 | Normal | Normal | Microcytic | | Parenchymal Liver Disease | Hypersplenism/DCLD |
| Y | | | Y | | | | 5.9 | 1.89 | 1400 | ymphocytos | 20000 | 89.9 | 31.2 | 34.7 | 17 | 84 | Normal | Normal | Normocytic | Acute Lymphocytic Leukemia | Normal | Acute Lymphocytic Leukemia |
| Y | Y | | Y | Y | | | 3.6 | 1.53 | 3600 | Normal | 80000 | 88.9 | 23.5 | 26.5 | 13.6 | 50 | Abnormal | Abnormal | Dimorphic | | Splenomegaly | Sepsis |
| Y | | | Y | | | | 2.3 | 1.23 | 1400 | Neutrophili | 39000 | 64.3 | 24 | 28 | 9 | 82 | Abnormal | Normal | Microcytic | Aplastic Anaemia | Normal | Aplastic Anaemia |
| Y | | | Y | Y | | | 3.8 | 2.37 | 2300 | Normal | 96000 | 64.6 | 16 | 24.8 | 15.3 | 70 | Normal | Normal | Microcytic | | Normal | Dimorphic Anaemia |
| Y | | | Y | | | | 4.4 | 1.72 | 3700 | Neutrophili | 9000 | 78.5 | 25.6 | 32.6 | 13.5 | 62 | Normal | Normal | Normocytic | | Normal | Sepsis |
| Y | | | Y | | | | 3.9 | 1.02 | 2200 | ymphocytos | 38000 | 118.6 | 38.2 | 32.3 | 12.1 | 55 | Normal | Normal | Dimorphic | | Normal | Dimorphic Anaemia |
| Y | Y | | Y | | Y | | 9 | 3.24 | 1700 | Neutrophili | 33000 | 76.3 | 22.7 | 29.8 | 32 | 20 | Normal | Normal | Microcytic | | Parenchymal Liver Disease | Hypersplenism/DCLD |
| Y | Y | | Y | | | | 6.8 | 2.3 | 2100 | Neutrophili | 13000 | 88.3 | 29.6 | 33.5 | 20.3 | 72 | Normal | Abnormal | Dimorphic | | Splenomegaly | Sepsis |
| Y | Y | | Y | | Y | | 9 | 4.2 | 1700 | Normal | 60000 | 82.1 | 22.4 | 27.3 | 33 | 125 | Normal | Normal | Dimorphic | | Parenchymal Liver Disease | Hypersplenism/DCLD |
| Y | | | | Y | | | 7.1 | 1.97 | 2400 | ymphocytos | 14000 | 104.1 | 36 | 34.6 | 20.5 | 110 | Normal | Normal | Dimorphic | | Normal | Dimorphic Anaemia |
| Y | Y | | | Y | | | 4.9 | 1.6 | 3000 | Normal | 21000 | 90.6 | 30.6 | 33.8 | 14.5 | 46 | Normal | Abnormal | Dimorphic | | Normal | Dimorphic Anaemia |
| Y | | | | | Y | | 5.4 | 1.4 | 2800 | ymphocytos | 24000 | 118 | 38.6 | 37 | 14.6 | 60 | Normal | Abnormal | Dimorphic | | Splenomegaly | Vitamin B12 Deficiency |
| Y | Y | | Y | | Y | | 5.2 | 1.46 | 1900 | ymphocytos | 13000 | 102.1 | 35.6 | 34.9 | 14.9 | 28 | Normal | Abnormal | Dimorphic | | Hepatomegaly | Megaloblastic Anemia |
| Y | | | | | Y | | 9.3 | 3.36 | 2900 | Normal | 28000 | 79.2 | 27.7 | 35 | 26.6 | 48 | Normal | Normal | Microcytic | | Splenomegaly | Infection |
| Y | | | | | | | 9.3 | 3.21 | 600 | Neutrophili | 53000 | 80 | 26 | 29 | 26.1 | 150 | Abnormal | Normal | Microcytic | Aplastic Anaemia | Normal | Aplastic Anaemia |
| Y | Y | | | Y | | | 7.5 | 2.27 | 1700 | ymphocytos | 92000 | 88.1 | 33 | 37.5 | 20 | 36 | Normal | Abnormal | Dimorphic | | Normal | Vitamin B12 Deficiency |
| Y | | | Y | | | | 6.7 | 2.25 | 3600 | Normal | 43000 | 94.7 | 29.8 | 31.5 | 28 | 155 | Abnormal | Abnormal | Macrocytic | | Hepatomegaly | Drug Induced |
| Y | Y | | | | Y | | 3.9 | 2.56 | 2600 | Normal | 43000 | 56.6 | 15.2 | 26.9 | 14.5 | 10 | Normal | Normal | Microcytic | | Splenomegaly | Myelofibrosis |
| Y | | | | | | | 5.8 | 2.14 | 2800 | Normal | 49000 | 85 | 27.1 | 31.9 | 18.2 | 24 | Abnormal | Normal | Dimorphic | | Medico Renal Disease | Drug Induced |
| Y | | | | | | | 8.4 | 3.63 | 3900 | Neutrophili | 60000 | 76.9 | 23.1 | 30.1 | 27.9 | 51 | Abnormal | Normal | Dimorphic | | Normal | Sepsis |
| Y | Y | | Y | | Y | | 5 | 2.51 | 1400 | Neutrophili | 14000 | 70.1 | 19.9 | 28.4 | 17.6 | 44 | Normal | Abnormal | Microcytic | | Splenomegaly | Hypersplenism/DCLD |
| Y | Y | | Y | | Y | | 3.8 | 1.45 | 2300 | Normal | 52000 | 81.4 | 26.2 | 32.2 | 11.8 | 27 | Normal | Normal | Dimorphic | | Splenomegaly | Hypersplenism/DCLD |
| Y | | Y | Y | | | Y | 8.1 | 2.49 | 2100 | Neutrophili | 25000 | 92 | 27 | 33 | 22.3 | 44 | Normal | Abnormal | Normocytic | Myelofibrosis | Hepatomegaly | Myelofibrosis |
| Y | | | | | | Y | 5.8 | 1.63 | 2900 | ymphocytos | 58000 | 104 | 30 | 37 | 17.2 | 49 | Normal | Normal | Macrocytic | | Hepatosplenomegaly | Vitamin B12 Deficiency |
| Y | | | Y | | | | 3.5 | 1.01 | 3700 | ymphocytos | 3000 | 100 | 35 | 35 | 10 | 62 | Abnormal | Normal | Dimorphic | | Normal | Megaloblastic Anemia |
| Y | | | | | | | 6.1 | 1.87 | 3300 | ymphocytos | 8000 | 93.6 | 32.6 | 34.9 | 17.8 | 62 | Normal | Normal | Macrocytic | | Normal | Infection |
| Y | Y | | Y | | | | 2.5 | 1.07 | 3100 | ymphocytos | 26000 | 108.7 | 36.2 | 33.3 | 7.5 | 84 | Normal | Normal | Macrocytic | | Hepatomegaly | Vitamin B12 Deficiency |
| | | | | | | | 9.9 | 4.02 | 2500 | Neutrophili | 55000 | 73.4 | 24.6 | 33.6 | 29.5 | 5 | Normal | Normal | Microcytic | | Hepatomegaly | Infection |
| Y | | | Y | | | | 2.8 | 0.68 | 1400 | ymphocytos | 18000 | 129.4 | 41.2 | 31.8 | 8.8 | 72 | Normal | Normal | Dimorphic | | Normal | Megaloblastic Anemia |
| Y | | | Y | | | Y | 5.1 | 2.97 | 2000 | Normal | 76000 | 65.3 | 17.2 | 26.3 | 19.4 | 70 | Abnormal | Normal | Microcytic | | Hepatosplenomegaly | Hypersplenism/DCLD |
| Y | | | Y | | | | 7.5 | 2.48 | 2600 | Normal | 40000 | 84.3 | 30.2 | 35.9 | 20.9 | 75 | Normal | Abnormal | Microcytic | | Normal | Chronic disease |
| Y | | | | | | | 6.6 | 2.05 | 2600 | ymphocytos | 6000 | 92.2 | 32.2 | 34.9 | 18.9 | 125 | Normal | Normal | Dimorphic | | Parenchymal Liver Disease | Hypersplenism/DCLD |
| Y | Y | Y | | | | | 4.8 | 1.68 | 2000 | ymphocytos | 25000 | 84.5 | 28.6 | 33.8 | 14.2 | 15 | Normal | Abnormal | Dimorphic | | Splenomegaly | Combined Nutritional Deficiency |
| | | | | Y | | | 9.9 | 4.03 | 3500 | Normal | 76000 | 71.1 | 24.8 | 34.8 | 28.7 | 50 | Normal | Normal | Microcytic | Combined Nutritional Deficiency | Normal | Combined Nutritional Deficiency |
| Y | Y | | Y | | Y | | 6.2 | 2.94 | 1200 | Normal | 41000 | 72 | 20 | 28 | 21 | 70 | Normal | Abnormal | Dimorphic | Haemophagocytic Lymphohistiocytosis | Hepatosplenomegaly | Dimorphic Anaemia |
| Y | | | | | | | 6 | 1.89 | 2300 | Normal | 42000 | 103.2 | 31.7 | 30.8 | 22 | 50 | Normal | Abnormal | Dimorphic | Micronormoblastic Erythropoiesis | Splenomegaly | Vitamin B12 Deficiency |
| Y | | | Y | | Y | | 5.4 | 1.77 | 2700 | Neutrophili | 58000 | 92.1 | 30.5 | 33.1 | 16.3 | 70 | Normal | Normal | Dimorphic | | Splenomegaly | Dimorphic Anaemia |
| Y | | | Y | | | | 3.3 | 1.83 | 2000 | Normal | 76000 | 64 | 17 | 26 | 13.5 | 50 | Normal | Normal | Microcytic | | Parenchymal Liver Disease | Hypersplenism/DCLD |
| Y | Y | | Y | | | | 4 | 0.95 | 2100 | ymphocytos | 7000 | 123.2 | 42 | 34.2 | 11.7 | 48 | Normal | Abnormal | Macrocytic | | Normal | Vitamin B12 Deficiency |
| Y | Y | | Y | | | Y | 2.7 | 1.5 | 3700 | Normal | 97000 | 59 | 18 | 31 | 8.6 | 30 | Abnormal | Normal | Microcytic | | Hepatosplenomegaly | Hypersplenism/DCLD |